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USE OF VITAMINS DURING ADAPTATION TO HIGH ALTITUDES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 3, May-Jun 84 (manuscript received 8 Jun 82) pp 4-9

[Article by M. S. Belakovskiy, N. G. Bogdanov, Ye. B. Gippenreyter and A. S. Ushakov]

[English abstract from source] The data obtained show that adaptation to a high altitude environment is accompanied by various metabolic changes. It is recommended to use essential nutrients--vitamins to optimize adaptation to this environment and to maintain adequate work capacity and good health.

[Text] The efficacy of acclimatization processes and man's work capacity depend on his vitamin supply [1-3]. At the same time, the following unfavorable states may occur at a high altitude: hypovitaminosis and avitaminosis, development of which may be due to alimentary insufficiency (low vitamin content in the diet, destruction of vitamins during storage and cooking, absence of optimum proportion of different vitamins, etc.); depression of normal intestinal microflora that produces certain vitamins (diseases of gastrointestinal tract and improper chemotherapy); impaired assimilation of vitamins of different etiology; increased vitamin requirement (large physical and mental loads, special climate conditions, etc.) [4]. All these factors must be taken into consideration when elaborating measures to prevent hypovitaminosis at high altitudes.

The desirability of greater vitamin intake in the mountains is attributable to the following circumstances: 1) when making high-altitude ascents, food consists chiefly of canned and freeze-dried products with low vitamin content; 2) intensive muscular activity in a hypoxic environment increases the body's vitamin requirements considerably; 3) most activities in the mountains (scientific expeditions, sports ascents, etc.) occur mainly in the summer, when the body most often experiences some vitamin deficiency that develops in the winter and spring; 4) the toxic effect of incompletely oxidized products (lactic and pyruvic acids, etc.) of interstitial metabolism in tissues, which occurs as a result of vitamin deficiency under hypoxic conditions, leads to metabolic disturbances.

There is usually a marked vitamin deficiency at the end of mountain expeditions. There is a very strong need for fresh vegetables and fruit. The leader of the Swiss expedition in 1952 or Mt. Everest, the physician Wyss-Dunant, admits that

he ate raw mushrooms and turnip greens, while paritipants who experienced a vitamin deficiency would surreptitiously pick green pomegranates on the way back, which no one wanted to sell them, although intake of synthetic vitamin C unquestionably protected them against scorbutic symptoms in the mountains [5].

Vitamin intake has a more beneficial effect when combinations of vitamins are used; however, this does not preclude the desirability of taking specific vitamins for regulation of a number of metabolic processes. Positive results were obtained from multiple vitamin intake in the form of lozenges in the mountains. Intake of ascorbic acid (vitamin C), vitamins B_1 (thiamin), PP (nicotinamide) and B_{16} (calcium pangamate) has specific effects. These vitamins increase work capacity, particularly in the case of muscular activity, which leads to an oxygen debt and is associated with working hypoxia.

Intake of multiple vitamins by the Soviet cross-country skiers at the moderate altitude of Squaw Valley shortened acclimation time, accelerated recovery processes after loads and was instrumental in better athletic achievement [6-7].

At the start of the English expedition on Mt. Everest in 1953, each member was given 100 multiple vitamin capsules containing the following: 5000 IU vitamin A, 500 IU vitamin D, 3 mg thiamin chloride, 2 mg riboflavin, 0.2 mg pyridoxine hydrochloride, 75 mg ascorbic acid, 20 mg niacinamide, 1 mg calcium panthothenate, 1 mg folic acid and 1 μg vitamin B_{12} [8-10].

The participants in the American expedition to Everest in 1963 took a set of vitamins daily. Multiple vitamins were not included in the mountain climbers' diet: a bottle of vitamin lozenges was available to everyone at mealtime, but the dosage was not regulated. However, two vitamins were a mandatory supplement to the daily food allowance, vitamin C and an R-A formula preparation. The author does not identify this product further. There is merely an indication that this formula dissolves well in water and elicits a high therapeutic response. It prevents depletion of vitamin reserve during vigorous exercise at a high altitude.

In the Khan Tengri expedition (6996 m), the climbers took 3-4 ordinary multiple vitamin lozenges per day during the stay in the mountains (1.5 months). Vitamin intake was not checked strictly. Each participant made 2-3 ascents ranked in category 5 of difficulty at altitudes of 6200-6995 m after systematic, gradual, relatively long (about 2 weeks) acclimatization and continuous vitamin intake.

During the main assault of Kahn Tengri, only 2 of the 20 climbers who reached the top presented distinct signs of mountain sickness (apathy, muscular weakness, impaired coordination, severe headache, dyspnea). The low incidence of moderate altitude sickness during such a technically difficult climb requiring much mental and physical stress is attributable to having the body's vitamin balance maintained while the climbers were at a high altitude (base camp was at 4500 m).

A. A. Aldashev et al. [11] found that supplemental intake of multiple vitamins (2 mg B_1, 2 mg B_2, 100 mg C, 20 mg PP, 50 mg P, 100,000 IU A and 100 mg E) and a specially recommended diet improved adaptation at altitudes of 1700, 2500 and 3600 m.

According to the data of Ya. I. Nevskiy et al. [12], the multiple vitamin product, Glutamevit, which contains 10 different vitamins, as well as glutamic acid and trace elements (calcium, phosphorus, iron, copper and potassium ions in the form of salt complexes), improved acid-base equilibrium in athletes at moderate altitudes (city of Przhevalsk, 1800 m above see level). It also

diminished metabolic acidosis after skaters were submitted to standard loads and pedaled as long as they could on a bicycle ergometer, as compared to a control group. The athletes took 2 Glutamevit tables twice a day after meals for 15 days. M. P. Ionina et al. [13] observed an analogous effect: daily intake of Glutamevit improved oxidative processes in the mountains, which increased the body's adaptibility for physical exercise at 2500 m altitude.

E. K. Mukhamedzhanov et al. [14], who examined mountain climbers who had made training ascents to over 4000 m in the Tyan Shan mountains for 2 weeks, found that intake of another multiple vitamin product, Decamevit, also diminished significantly manifestations of metabolic acidosis.

V. P. Pashchenko et al. [15] report on the beneficial effect of the Aerovit multiple vitamin product on the functional state of individuals engaged in physical labor in the Extreme North. According to the findings of R. F. Sidorenko et al. [16], 30-day intake of this product, at the rate of 1 lozenge per day, had a beneficial effect on biochemical processes in track and field athletes, accelerating recovery after a measured exercise load on a bicycle ergometer. Aerovit is recommended as a supplement for individuals who eat canned and freeze-dried products for long periods of time and are exposed to extreme factors.

It is believed that the protective effect of multiple vitamins consists of maintaining oxidative processes on a high level, which prevents a change in metabolism to the less efficient anaerobic route of energy production.

According to the studies of F. P. Kosmolinskiy [17], I. M. Khazen [18] and other authors, human and animal resistance to hypoxia increases with intake of some vitamins (thiamin, ascorbic and paraaminobenzoic acids, riboflavin, citrin). In this regard, vitamin E is of interest, and the desirability of its supplemental use at high altitudes has been discussed repeatedly. Vitamin E has long since attracted the attention of researchers, with regard to investigating its possible effect on increasing work capacity and resistance to hypoxia. This is attributable to three reasons: 1) animal experiments revealed that a vitamin E deficiency leads to development of muscular dystrophy, and for this reason the requirement for it apparently increases when performing heavy and prolonged exericse; 2) data have been obtained to the effect that animal resistance to hypoxia and hyperoxia changes under the influence of vitamin E, and this is attributed to its capacity to have in vitro and in vivo activity as an antioxidant [19, 20]; 3) the vitamin could have a beneficial effect on lowering the load on the circulatory system during stressful athletic activities, since such an effect has been observed in the treatment of some diseases related to functional defects of the heart and circulation [21]. Prokop [22-23] found that intake of vitamin E causes faster recovery following standard physical loads. V. M. Braginskiy and M. M. Mirzoyev [24], as well as Curto [25], believe that vitamin E increases work capacity and resistance to hypoxia. A. M. Alekseyeva and A. V. Tkachenko [26] report on the preventive effect of vitamin E in the presence of some forms of hypoxia. They found that vitamin E prevents and retards changes in hemodynamics, structure and chemistry of reproductive glands, heart and kidneys of rats. However, Thomas [27] failed to demonstrate a reliable difference between indicators of the cardiorespiratory system and motor tests with intake of this vitamin, as compared to the control.

In view of the contradictory data concerning the effects of vitamin E, Sharman et al. [28-29] made special studies of adolescent swimmers, using the double-blind control method. The subjects were divided into two equal groups, similar in anthropometric and other parameters. One group was given 2 tablets of α-tocopherol acetate (200 mg) daily, in addition to their normal diet, for 6 weeks of training and the other received a placebo. The results of this study revealed that there was reliable improvement of physiological functions and work capacity in both groups of swimmers under the influence of training. The hypothesis was advanced that vitamin E could have had a beneficial effect if the subjects had been highly trained. Sharman et al. [30] organized analogous study, but on high-class swimmers who swam 40,000-50,000 m daily. The dosage, time and method of investigation were analogous to those used in the preceding study. Analysis of the results again confirmed the presence of changes attributable to training, but failed to demonstrate statistically reliable changes that would be indicative of the ergogenic (i.e., increasing work capacity) effect of vitamin E.

A. A. Vakhidov [31] found that α-tocopherol prevents decrease in phospholipids of liver and kidney tissues of rats kept for 2 months in the Pamirs (4000 m). Intramuscular injection to the animals of this agent (5 mg/100 g weight every 5 days) elicited a beneficial effect at the early stages of adaptation to high altitude.

In the opinion of Singh [32], intake of vitamin E at high altitudes helps maintain normal functional activity of the body. Animal (rats, rabbits) survival under hypoxic conditions at low atmospheric pressure was higher when they were given vitamin E than in animals who experienced a vitamin E deficiency. They determined that the force of contraction of pigeons' respiratory muscles is determined by the amount of vitamin E given to the birds with their feed. In the case of vitamin E deficiency in adult humans, there may be hemolysis of red blood cells, creatinuria, weight loss and impaired absorption of fats. Singh expresses his regret that there was no special use of vitamin E in any of the mountain-climbing expeditions.

Japanese physicians tested the effect of vitamin E on achievement of long-distance runners at moderate altitudes. Two groups of athletes started a 4000-m heat on Honshu. One group of runners took vitamin E regularly for several weeks before the heat. They reached the finish line 30 s sooner than the track and field athletes who took no vitamin E. The heats were repeated several times with similar results. After this, it was decided to use vitamin E in training Japanese Olympic athletes for the competitions in Mexico (2240 m).

It was shown that B group vitamins increase the activity of respiratory enzymes, which in turn results in better uptake of oxygen by tissues, and as a result resistance to hypoxia improves [34].

During ascent of Broad Peak (8047) without oxygen gear, Austrian climbers took vitamin B_{12} tablets daily, which intensified hemopoiesis [35].

Several authors have voiced the opinion that pangamic acid improves oxygen uptake in the presence of systemic and local hypoxia. They relate this to its effect on processes of utilization of glucose and activity of some enzymes of tissue respiration, in particular, succinate dehydrogenase [34, 36, 37 and others].

Data have been accumulated to date indicative of the desirability of using in the mountains such a means from the arsenal of megavitamin prophylaxis and therapy as intake of large amounts of ascorbic acid, although the mechanism of its action has not yet been sufficiently investigated. In the first place, it was shown that increased ultraviolet radiation causes considerable loss of ascorbic acid due to its intensified metabolism and elimination. As a result, vitamin C deficiency may develop, which causes adverse biochemical and morpho-functional changes (depression of secretory and excretory function of the stomach, decrease in digestive potency of gastric juice, etc. [38]), whereas supplemental intake of ascorbic acid has a protective effect in this regard. In the second place, reliable findings have been made on the efficacy of high doses of ascorbic acid for prevention and treatment of colds and certain other diseases [39]. In the third place, there is information to the effect that ascorbic acid has an indirect antistress effect [39]. In this regard, it is opportune to recall that intense solar radiation (particularly in the ultraviolet region of the spectrum) and low temperatures are factors inherent in a high-altitude environment, which have a stressor and, occasionally, extreme effect on the body.

Several hypotheses have been expounded [39, 40] to explain the mechanism of action of ascorbic acid. The efficacy of large doses of ascorbic acid in the prevention and treatment of acute respiratory diseases, influenza, pneumonia and some other diseases is attributed to increased synthesis and activity of interferons, which counteract penetration of viruses into health cells, its antioxidant action, as well as the fact that ascorbic acid is a physiological inhibitor of hyaluronidase [39].

L. Pauling [39] recommends taking 250 mg to 10 g ascorbic acid per day. In his opinion, the optimum dosage is 1 g (250 mg, 4 times a day at mealtime). The dosage should be increased when overtired due to physical labor and lack of sleep, as well as when there is contact with cold victims.

However, in the opinion of N. I. Yalova et al. [41], it is hardly desirable to take large doses of vitamin C in sports practice, since this is an additional burden on the body against the background of very intense physical and neuro-emotional stress. These authors believe that intake of ascorbic acid in a dosage of 150-200 mg/day for 20 days, in conjunction with other vitamins, provides an adequate supply of ascorbic acid for the body.

A beneficial effect can also be obtained in the mountains from intake of galascorbin, which is a combination of sodium salts of ascorbic acid and tannin. This product has vitamin P and C properties, enhances the body's resistance to hypoxia, muscle tone and muscle work capacity, normalizes energy metabolism and stimulates processes of tissue regeneration. It is recommended for intake by mouth, with the same indications as ascorbic acid with vitamin P, i.e., 0.5 g 3-4 times a day 1 h before meals, for 20-40 days [42].

In view of the advanced hypothesis that carotenoids are involved in intracellular deposition of oxygen (high concentrations of carotenoids were demonstrated in organs of high-altitude animals, they are responsible for hemopoiesis and delivery of oxygen to tissues [43]), it is tempting to investigate the efficacy of these compounds, which change into vitamin A in the body, when used

for preventive and therapeutic purposes in the presence of hypoxia (particularly when it is acute).

A. A. Altymyshev recommends use of "gipkos" during mountain expeditions. One lozenge of this product contains lyophilized sea buckthorn [Hippophae] juice (58-68%), saccharose (30-35%), lactose (3-5%) and honey-sugar-sea buckthorn syrup (2-3%). Lyophilized sea buckthorn juice contains a natural complex of biologically active substances: water- and lipid-soluble vitamins and provitamins (C, B_1, B_2, B_c, E, K, choline, betaine, bioflavonoids, carotenes, carotenoids, coumarins, tannin, organic acids, a wide assortment of amino acids including 50% of the essential ones and fatty fruit pulp butter with high unsaturated fatty acid content). The lozenge also contains trace elements. Gipkos is also indicated for atonia, sluggishness and inhibition as a means of help in recovery after large burdens, having general fortifying and toning effects. It is taken at the rate of 2 lozenges 3 times a day, 20-30 min before meals. There are no limits to a course.

N. N. Yakovlev and L. G. Leshkevich recommend enrichment of the diet with fruit and vegetables (with somewhat decreased fat content), as well as vitamins A, B_1, B_2, PP, C and E in amounts considerably greater than used in the lowlands in order to accelerate the process of adaptation to high altitudes in athletes [7].

Daily intake of a wide assortment of vitamins (B_1, B_2, B_6, B_{12}, B_{15}, PP, C) combined with folic acid, iron glycerophosphate and methacil [4-methyluracil] increased the red blood cell count and hemoglobin, oxygen capacity of blood, was instrumental in more effective acclimatization processes and enabled oarsmen and fencers who met at an altitude of 2500 m to better endure physical loads and regain athletic work capacity faster [44].

Thus, the data we have submitted are indicative of the important role of vitamins in the process of adapting to the extreme conditions of high altitudes, in maintaining a high level of work capacity and safeguarding health as a whole.

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EXPERIMENTAL AND GENERAL THEORETICAL RESEARCH

UDC: 612.172.014.422-08

RELIABILITY AND EFFICIENCY OF KUBICEK RHEOGRAPHIC METHOD FOR MONITORING CARDIAC OUTPUT AND STROKE VOLUME

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 3, May-Jun 84 (manuscript received 19 Apr 83) pp 9-14

[Article by A. M. Genin, L. S. Zingerman, D. G. Maksimov, G. Ye. Belozerov, V. P. Katuntsev, M. V. Obukhova, K. S. Yurova, G. I. Kheymets, V. A. Galichiy and R. I. Finogenova]

[English abstract from source] Simultaneous measurements by the Fick direct method and the Kubicek rheographic method of cardiac output of 20 men with ischemic heart disease have shown that both methods are well correlated ($r = 0.76$, $k = 0.92$, $n = 41$). The reproducibility of the Kubicek data was slightly better than the Fick data (on the average ±6% instead of ±9-10%). An attempt of increasing the correlation of the Kubicek data with the Fick data by correcting the specific resistance with respect to the hematocrit data and the chest perimeter failed. In order to provide the necessary accuracy of the Kubicek method, it is required that the procedure be stringent and the five variables in the formula for calculating cardiac output be precisely measured. The cardiac output values determined simultaneously by the Kubicek method and by x-ray contrast ventriculography showed a better correlation ($r = 0.88$, $k = 0.97$, $n = 15$).

[Text] In view of its advantages, the rheographic method of measuring cardiac output and stroke volume has gained wide use in clinical practice and scientific research [1-4]. However, the question of correlation between this method with conventional ones and, in particular, invasive methods remains debatable [5-8].

Our objective here was to assess the reliability and efficiency of Kubicek's rheographic method [9] by comparing it to the direct method of Fick [10] and contrast ventriculocineradiography [11, 12], and to estimate the corrections for the Kubicek method by considering hematocrit [13] and chest perimeter of the subjects [14, 15], as well as to estimate the margin of error of the Kubicek method as a function of margin of error in measuring physiological parameters contained in the formula for calculating stroke volume (SV).

Methods

The Kubicek rheographic method involved use of the RPG2-02 tetrapolar rheoplethysmograph. To improve accuracy of measurement of the base interelectrode resistance (R_{bas}, Ω), the signal from the input of the rheograph dial was fed to a V-7-22A digital voltmeter, which was calibrated according to the R-33 resistance box. The potential electrodes were placed by the Kubicek method in the bottom part of the neck and on the level of the xiphoid process. Active electrodes were placed on the forehead and on the level of the subjects' waist [4, 14]. The width of the circular electrodes was 7 mm. For closer contact with the body surface, the electrodes consisted of individual segments attached to a flexible rubber band, the ends of which were joined with a velcro fastener. The distance between potential electrodes (L, cm) was measured from the bottom edge of the neck electrode to the top edge of the chest electrode. Volumetric and differential rheograms were recorded simultaneously with the EKG, and mean-frequency PKG [phonocardiogram] on an 8-channel Mingograph. The amplitude of the differential rheogram (Ad) was measured from the center of the sinus-wave calibration signal to the peak Ad. To calculate SV, we took the Ad (mean), for which purpose we measured Ad for 2-3 respiratory cycles. We determined the start of the period of expulsion of blood from the heart (T_e) from the point of fusion of the ascending part of the anacrotic wave with its tangent, while the end of the expulsion period was determined from the peak of the first high-amplitude oscillation of the second PKG tone. The PKG sensor was situated over the projection of the pulmonary artery. The end of the period of expulsion of blood from the heart determined in this manner was 0.02 s ahead of the negative peak of the differential rheogram in most cases. To calculate SV, we took the T_e(mean) value in the same complexes as for determination of Ad (mean). Heart rate (HR) for determination of cardiac output (MV) [minute volume of circulation] was determined from the mean value for the (RR_{EKG}) interval during the period of measurement of Ad and T_e. Rheograms were recorded before starting the angiographic tests, after catheterization of blood vessels and cavities of the heart, when drawing blood samples for the Fick method, during ventriculocineradiography, during coronography, when blood was drawn again for the Fick method and after termination of angiographic studies.

The Fick method was used in its standard version [10]. Partial oxygen tension and pH of blood samples from the left ventricle and pulmonary artery were measured using an AVL-940 instrument and checked concurrently by means of the micro-Astrup instrument. Hemoglobin was assayed by the cyanmethemoglobin method. Pulmonary ventilation (PV) and oxygen uptake by the subjects were checked with an MMC metabolometer of the Beckman firm. Hematocrit was determined by the conventional method. Ventriculocineradiographic measurement of stroke volume was made by the method of Dodge [11] as modified by L. S. Zingerman [12].

The above tests were performed on 20 men suffering from ischemic heart disease and, in most cases, with a history of myocardial infarction. They ranged in age from 33 to 58 years. Their weight was 56-98 kg and height 164-185 cm.

The results of the tests were submitted to conventional statistical processing.

Results and Discussion

A comparison of the results of 41 simultaneous measurements of cardiac output by the direct Fick method and rheographic method of Kubicek revealed that there is a rather high correlation between them: the coefficient of correlation (r) was 0.76, while the coefficient of regression was 0.92 (Table 1). The Figure, which shows the variability of paired correlations between the two methods, also illustrates the closeness of data obtained by the two methods. The Figure shows that the difference in these relations is mainly contained in the range of ±25% scatter from a line plotted on the basis of a regression equation characterizing the relationship between the two methods. Table 1 shows that only 7% of all cases deviated by more than 25% from the data obtained by the Fick method. The maximum deviation of 41% occurred in only 1 case. The mean deviation of MV found by the Kubicek method from data obtained by the Fick method constituted 13%, whereas the difference between mean values for MV obtained by both methods constituted only 3% (see Table 1).

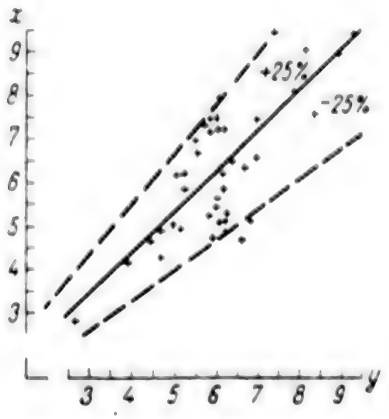
Table 1. Comparison of MV values obtained by the direct Fick method and rheographic methods

PARAMETER	METHOD OF MEASURING MV				
	FICK	RHEOGRAPHIC METHODS			
		KUBICEK		PUSHKAR' ET AL. (1980)	GUNDAROV ET AL. (1983)
		$\rho = 150$	ρ_{Hct}		
	x	y	z	γ	β
$M \pm m$. ML	6245±236	6050±195	7038±314	6164±214	5909±186
$M_y(Z, \gamma, \beta) - M_x$ ML		−195	+793	−81	−336
%		−3	+13	−1	−5
INDIVIDUAL DEVIATION, %					
MEAN		±13,0	±22,0	±15,7	±13.4
MAXIMUM		+41	+65	+37	+36
		−24	−25	−35	−31
% DEVIATION FROM Mx					
TO 15		62	35	53	59
16—25		31 } 93	41 } 76	20 } 73	27 } 86
26 - 35		3,5	10	22	12
OVER 35		3,5 } 7	14 } 24	5 } 27	2 } 14
CORRELATION COEFFICIENT $r_x(y, z, \gamma, \beta)$		0,76	0,73	0,63	0,71
REGRESSION COEFFICIENT $K_x(y, z, \gamma, \beta)$		0,92	0,76	0,70	0,90
REGRESSION EQUATIONS		$x=0,92 \cdot \gamma + 679$; $x=0,90 \cdot \beta + 927$;		$x=0,76 \cdot Z + 819$. $x=0,70 \cdot \gamma + 1930$.	

Note: There were 41 readings by each method; MV measured by the Fick method was taken as 100%; ρ_{Hct} is specific resistance of blood corrected in accordance with hematocrit readings: $\rho = 56.8 \cdot e^{0.025Hct}$ (Geddes and Costa, 1973).

In order to correctly assess the results, one must consider the margin of error of each method. According to the literature, mean margin of error is ±10% for the Fick method, but there can be deviations of 20-30% and sometimes

more [16, 17]. Our determination of the margin of error of the Kubicek method provided there is an error in measuring the distance between electrodes or displacement of electrodes by about 1 cm revealed that the margin of error in value of MV constitutes a mean of ±8%. An error in measurement of R on the order of 1 Ω yields a mean margin of error of ±8.2%. Error in measuring the amplitude of the differential rheogram of 2 mm (1 mm in measuring isoline level and 1 mm on amplitude) yields an error of ±10%. An error of 0.02 s in measuring time of blood expulsion from the heart yields an MV error of an average of ±7.5%, while error in determination of HR on the order of 2/min yields an error of ±2.6%. Overall maximum error in this case would be ±36.3%, which is approximately consistent to the maximum differences between MV when measured by the Fick and Kubicek methods.



Relationship between MV values measured by Fick and Kubicek when determined simultaneously.
X-axis, MV according to Kubicek (in liters); y-axis, MV according to Fick (liters)

In view of the fact that in our studies we made simultaneous determinations of MV by the two above-mentioned methods a second time, at an interval of 1-2 min, in the presence of virtually stable HR, PV and oxygen uptake, it was possible to assess the reproducibility of both methods. We found that mean deviation of MV values is 9% with the Fick method and 6% with the Kubicek method. Maximum deviation reached 15-19% with the Fick method and 13-16% with the Kubicek method. The number of cases with deviations of MV from base value of less than 10% constituted 50% for the Fick method and 75% for the Kubicek method (Table 2). Thus, the reproducibility of the Kubicek method is no worse, and even somewhat better than of the direct Fick method. However, if an additional error appears for one of the five variable parameters contained in estimation of MV according to Kubicek, the margin of error of the method could increase appreciably.

In order to assess the means of possibly increasing the correlation between the Kubicek and direct Fick methods, we tested the influence of correcting specific resistance of blood according to hematocrit readings [13], as well as correction of MV according to Kubicek by considering the perimeter of the subjects' chest [14, 15]. As can be seen in Table 1, this did not increase the correlation between data obtained by the two methods, although we had previously noted some rise of coefficient of correlation (by 0.10-0.16) in a study of essentially healthy subjects (n = 31).

A comparison of MV values found by the rheographic method of Kubicek to contrast ventriculocineradiography revealed a high correlation between them (r = 0.88; k = 0.97; Table 3). In 80% of the cases, infusion of contrast medium into the left ventricle is associated with an average increase of 28% in MV ($P<0.05$; and mainly due to increase in stroke volume of the heart); in about 20% of the cases, the opposite reaction was demonstrated. As a result, there was an extremely low correlation between MV values found by ventriculocineradiography and those

found by the method of Fick or Kubicek 7-10 min prior to infusion of contrast medium (see Table 3).

Table 2. Mean MV values and possible individual variability of MV when measured repeatedly at 1-2 min interval with subjects in stable state

PARAMETER	METHOD OF MEASURING MV	
	FICK	KUBICEK
M_M, ML	6187	6119
MEAN DEVIATIONS	±537	±398
ML	±9	±6
%		
MAXIMUM INDIVIDUAL DEVIATIONS		
ML	+911	+758
	−1381	−1160
%	+15	+13
	−19	−16
MV DEVIATIONS OF LESS THAN 10%, %	50	75
MV DEVIATIONS OF 10% OR MORE, %	50	25

Note: MV was measured a second time by the Fick and Kubicek methods in 16 cases.

Table 3. Comparison of MV values found by contrast ventriculocineradiography (VG), the direct Fick method 7-10 min before ventriculography and rheographic method of Kubicek before and during ventriculography

PARAMETER	METHOD AND TIME OF MEASURING MV			
	FICK 7-10 MIN BEFORE VG	KUBICEK 7-10 MIN BEFORE VG	KUBICEK DURING VG	VG
	y	z	y	x
$M \pm m$, ML	6262±451	5952±360	7700±742	8040±816
MEAN DEVIATION FROM M_X				
ML	−1786	−2096	−318	
%	−22	−26	−4	
% DEVIATION FROM M_X				
TO 15	20	13	92	
16—25	3 } 33	13 } 26	8 } 100	
26—35	27	40		
OVER 35	40 } 67	34 } 74		
MAXIMUM INDIVIDUAL DEVIATIONS FROM M_x, %	+65	+67	+13	
	−88	−58	−22	
$r_x(y, z, \gamma)$	0,14	0,24	0,88	
$K_x(y, z, \gamma)$	0.23	0,48	0,97	
REGRESSION EQUATIONS	$x=0,97 \cdot y+579$; $x=0,48 \cdot Z+5191$; $x=0,23 \cdot \gamma+6608$			

Note: There were 15 cases; MV found by ventriculography was taken as 100%.

Interesting data were obtained by the Kubicek method about the influence of angiographic tests on MV value. According to these data, catheterization of great vessels and chambers of the heart was associated with some increase in pulse rate and an average of 12% increase in MV. Coronarography was usually associated with 5-15-s slowing of HR and decrease in MV (to 1/3 to 1/2 in some cases), followed by approximately the same increase in MV with regard to time, with subsequent decline and stabilization. After concluding the angiographic tests, HR was about the same as before they were started (mean of 85 and 83/min). The values of MV found by the Kubicek and Fick methods increased after angiography by 17 and 20%, respectively ($P<0.1$) due to increased stroke volume. Concurrently there was a 14% increase in pulmonary ventilation ($P<0.1$).

Thus, there was rather good correlation between data on MV values obtained by the rheographic method of Kubicek and those obtained by the Fick method, under both conditions of relative calm and after angiographic studies. An even higher correlation was noted between the Kubicek method and contrast ventriculocineradiography. We should call attention to the need to adhere to a precision of studies of all five variables contained in the calculation of MV values according to Kubicek. The coefficient of correlation of the rheographic method of Kubicek with invasive direct methods will be about 0.80.

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WALKING ERECT AS A FACTOR IN DEVELOPMENT OF ARTERIAL HYPERTENSION IN PRIMATES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 3, May-Jun 84 (manuscript received 4 Apr 83) pp 14-19

[Article by G. S. Belkaniya and V. A. Dartsmeliya]

[English abstract from source] Time-course changes in the cardiovascular function of rhesus monkeys were investigated during forced orthograde statics and upright walking. Arterial pressure by Korotkoff sounds (in certain cases by a direct method in the femoral artery) and major parameters of central hemodynamics by tetrapolar thoracic rheography were measured. The monkeys developed stable arterial hypertension 3 months after the onset of the upright study. Hemodynamic parameters reflected circulation centralization, formation of the hyperkinetic type of the orthostatic reaction and development of arterial hypertension of the resistive type. It is suggested that orthostatics may contribute to the development of arterial hypertension.

[Text] The conception of relevance of orthostatic position as the phylogenetic basis of potentiating the pressor reaction of the cardiovascular system (CVS) and role of orthostatism in development of hypertension in primates, including man, was formulated on the basis of many years of investigation of the main physiological systems of the body as related to orthostatic position [1-5]. The following group of facts served as grounds for formation of this conception.

The general trend of all phylogenetic and ontogenetic changes in reactive properties of the CVS that have been observed is refinement and intensification of function of pressor mechanisms implemented by both reflex and humor factors. According to summary data [6], the increasing representation of pressor reactions in higher mammals, unlike phylogenetically earlier animal species, was manifested by the fact that a depressor effect of changes in blood pressure was observed in 28% of the cases and a pressor effect in 72% after stimulation of mechanoreceptors and chemoreceptors of internal organs, skin and muscles.

There is distinct demonstration of correlation between the change to orthograde equilibrium and intensification of pressor features in regulation of the CVS in phylogenesis and ontogenesis [2]. Functional changes in several physiological systems and, first of all, the CVS that provided for the body's adaptation to earth's gravity are the basis of improvement of pressor mechanisms of controlling circulation.

Sensitivity to pressor amines (epinephrine, norepinephrine) increases and sensitivity to hypotensive agents (acetylcholine, histamine and serotonin [7]) in orthostatic position; there is also decrease in vasodilating and increase in vasoconstrictive reactions [8, 9].

In rats submitted to permanent fixation in erect position with the head up (5 h/day), in addition to immobilization, developed arterial hypertension, in contrast to animals immobilized in horizontal position [7, 10].

Analysis of clinical data on arterial hypertension in humans showed increased activity of expressly the systems regulating vascular tonus and hemodynamics, which are constantly in a state of tonic activity directed toward compensation of hydrostatic changes, when no disease is present [2].

A comparison of the above facts led us to the conclusion that orthostatic position is a real and substantial factor that potentiates the pressor reactions of the CVS. This conclusion served as the basis for a formulated working hypothesis: the phylogenetic basis of formation of hypertension in man is a set of antigravity reactions of the body formed through evolution and fixed in ontogenesis.

In view of the foregoing, the objective of our investigation was to examine the direction of functional changes in the CVS under experimentally produced orthograde conditions, with the monkeys walking erect.

Methods

The studies were conducted on 5 experimental and 5 control Macaca rhesus males 3.5-4 years of age. For the direct experiment to demonstrate the significance of orthostatic position to potentiation of pressor adjustment of CVS regulation and development of arterial hypertension, we developed a model of experimental biped walking. For this, we used an immobilization method: using special overalls, the animals were deprived of the ability to use their upper limbs for locomotion, even when moving on the floor. Under experimental bipedal conditions, the monkeys were kept in a cage in a group for 240 days (the experiment is still continuing at this time).

Systolic (BP_s) and diastolic (BP_d) blood pressure (BP) was measured by the Korotkov cuff method; central hemodynamics were evaluated by means of tetrapolar thoracic rheography. We determined stroke, minute and cardiac output and accordingly calculated the stroke (SI) or systolic and cardiac (CI) indexes, total and specific (SPR) peripheral resistance of vessels, determined mean BP ($BP_m = BP_d + 0.42\ BP_{pulse}$) and heart rate (HR, per min).

BP was measured daily; tetrapolar thoracic rheography was performed at different periods determined on the basis of analysis of dynamics of changes in general BP level, at rest (the animals were immobilized in horizontal position), and the orthostatic test was performed at such periods also. Background parameters of the monkeys were measured after prolonged (2-3 months) adaptation to experimental conditions (taking and immobilizing the animals). Concurrently with the main experiment, we observed control animals of the same age.

The orthostatic test was performed by the standard method [2]; the analyzed parahemodynamic parameters were analyzed in the background period (horizontal position on turntable) and in the 1st, 2d, 3d, 4th, 5th, 10th, 15th and 20th min of orthostatic position. Considering that, in monkeys, the orthostatic reaction becomes stabilized within a few min, we estimated the mean value of the hemodynamic parameters considered for all periods of recording.

Circulating blood and plasma volumes, hematocrit and glomerular renal filtration were measured by the dye-dilution method [11] by the method of Kunes, Capek and Jelinek in the 3d month of the bipedal period.

Results and Discussion

The results of the studies revealed that a high BP was demonstrable in all biped monkeys 3 months after changing them to orthograde conditions and erect walking, and it persisted for the next 8 months. Throughout the observation period there were similar phasic dynamics to the individual BP changes. We thus were able to single out four periods of changes in general BP level (Figure 1).

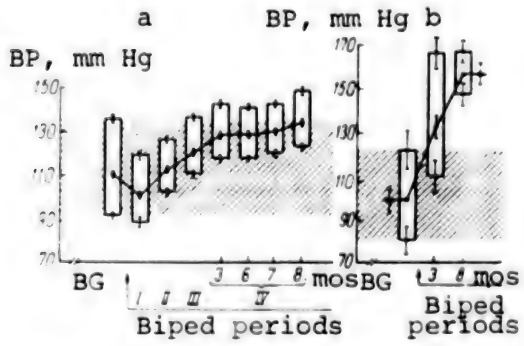

Figure 1.
Dynamics of BP changes in monkeys at different periods of experimental bipedia [BG--background]
a) phases of BP changes in biped monkeys
b) BP check in biped monkeys under nembutal anesthesia

The first period, which lasted up to 8-9 days, was characterized by reliable decline of BP_s, BP_d and BP_m. In the second period, 40th to 60th days and, in one of the biped monkeys starting on the 10th day, BP_d was stabilized at the base level or higher. BP_s continued to be lower than the base level.

In the third period, BP_d rose progressively, while BP_s corresponded to base values. In the fourth period, starting on the 80th-85th day and to the present time (240 days), BP_s, BP_d and mean dynamic BP were significantly and reliably above the base levels.

BP was measured by the direct method in the femoral artery and indirect method under nembutal anesthesia as a check in the fourth period, in biped and control animals under concurrent observation (see Figure 1). The purpose of this examination was to determine the basis of the high BP in the bipeds: functional hyperreactivity of the CVS or an established hypertensive mode of regulation? The readings taken in the 3d month of bipedia revealed that, unlike control animals whose BP dropped under anesthesia as compared to background values, biped monkeys showed persistence of high BP. While background mean values constituted 124±6 mm Hg for BP_s, 95±5 for BP_d and 107±5 for BP_m, the bipeds presented 167±6, 110±5 and 133±4 mm Hg, respectively. There were even more marked differences between biped and control monkeys when BP was measured under anesthesia in the 8th month of walking erect. In control animals BP_s (114±4 mm Hg), BP_d (90±4) and BP_m (100±4) corresponded to the normal range but in biped monkeys BP rose even more: BP_s 167±6, BP_d 149±8 and BP_m 157±7 mm Hg.

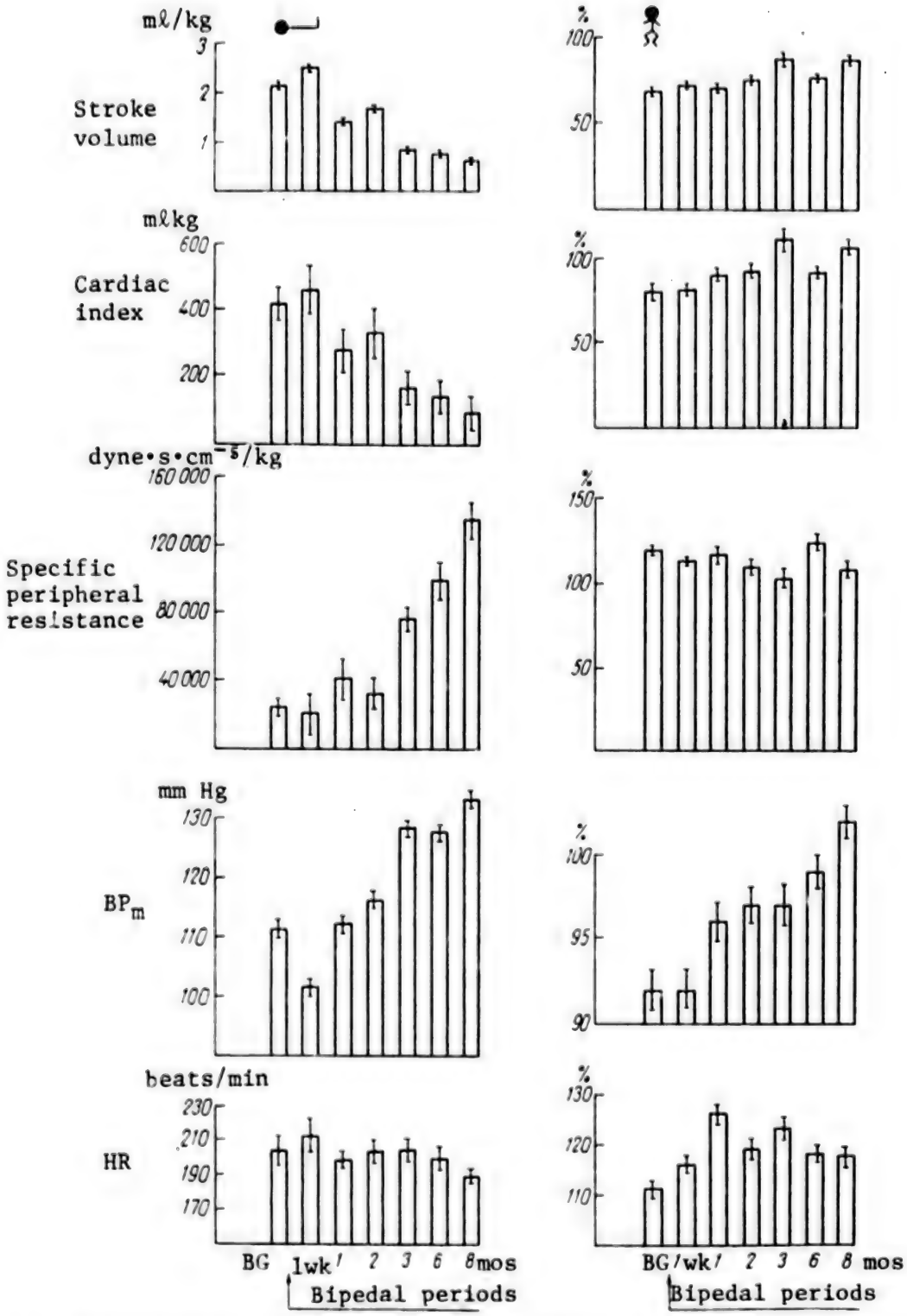

Figure 2. Characteristics of central hemodynamics of monkeys in horizontal position (left) and during 20-min orthostatic test (right) in different periods of experimental bipedia (values of parameters in horizontal position taken as 100%); BG--background

Formation of persistent arterial hypertension in the biped monkeys corresponded to typical changes in central hemodynamic parameters: progressive decline of cardiac output and stroke volume, elevation of BP_m and increase in specific peripheral resistance (Figure 2).

The dynamics of functional changes in the CVS of biped monkeys during the orthostatic test, as BP stabilized at a high level, also indicated increasing centralization of circulation (see Figure 2), which is consistent with current clinical conceptions of onset of essential hypertension [12]. The biped monkeys showed a change to hyperkinetic type of reaction during the orthostatic test: increase in cardiac output and stroke volume, as well as HR and more marked stabilization of BP_m throughout the period of orthostatic testing.

Thus, the hemodynamic characteristics in horizontal position and during the orthostatic test were indicative of the fact that increased peripheral vascular resistance was the basis of the high BP in biped monkeys, i.e., they developed arterial hypertension of the resistive type. This conclusion was also confirmed by the data referable to fluid balance (see Table). Along with decline of circulating blood volume and plasma volume, the biped monkeys presented redistribution of fluid from the vascular bed to the interstitial space, as well as diminished renal glomerular filtration.

Indicators of fluid balance and renal glomerular filtration in control and biped monkeys

Parameter	Control $\bar{X} \pm S_{\bar{X}}$ (Δx)	Bipeds $\bar{X} \pm S_{\bar{X}}$ (Δx)
Hematocrit (Ht)	43,0±0,3 (42—44)	41,4±0,2* (41—42)
Plasma volume (PV)	52,4±2,3 (47,9—57,8)	47,8±0,7* (45,6—50,7)
Extracellular fluid volume (ECFV % BW)	33,8±2,3 (29,9—41,7)	34,0±4,5 (31,1—39,9)
Dilution coefficient (Q_{ECT})	0,185±0,008 (0,161—0,205)	0,165±0,005* (0,146—0,180)
Renal glomerular filtration (GFR), mℓ/min/kg	4,5±0,2 (3,6—4,9)	3,9±0,3 (2,96—4,8)
% ECFV/min	1,34±0,11 (1,09—1,59)	1,18±0,14* (0,8—1,5)
BP_s	124±6 (103—137)	167±5* (153—187)
BP_d	81±4 (67—87)	110±5* (107—130)
BP_m	99±5 (83—107)	133±4* (120—150)

* $P<0,05$.

The experimental biped model reproduces the conditions for onset of the main physiological consequence of orthograde statics in hemodynamics: redistribution of most of the blood volume in vessels below the level of the heart. As a result of elevated hydrostatic pressure and greater redistribution of blood volume over hydrostatic and functional gradient to the vascular system of the lower limbs [2], there is decreased venous return to the heart which, in turn, leads to decrease in cardiac output and stroke volume. Such a hemodynamic

situation is the basis for triggering and intensification of the pressor mechanism of CVS regulation.

This situation, which is based on normal neurohumoral regulation, could be a strong triggering mechanism for development of arterial hypertension if exposure to orthostatic factors is frequent and long enough. Development of arterial hypertension in the biped monkeys is indicative of the likelihood of such a possibility.

In this regard, it is opportune to quote the assumption of B. Folkov and E. Nil [13]: "... that simply normal central neurohormonal factors are an important triggering mechanism (of arterial hypertension--Belkaniya and Dartsmeliya), if they occur quite often" (p 459). However, as in most of the other conceptions of etiology and pathogenesis of arterial hypertension, this role is attributed to psychoemotional stress.

Without denying the significance of the latter, we believe that orthostatics, an inseparable and most consistent condition of man's normal vital functions, is the most probable factor that constantly maintains pressor regulation of BP in man, which is capable of changing this regulation to a hypertensive mode. And, although R. Rashmer [14] stresses that man spends most (2/3) of his life in erect position, in his monograph, "Dynamics of the Cardiovascular System," he limits himself only to consideration of mechanisms of regulation of circulation in this position, without making any extrapolation to the mechanism of development of arterial hypertension.

At the same time, historically there was considerable increase in man's exposure to the orthostatic factor (increase in mean life span, longer active phase per day, in both adults and children, work in shifts, etc.). This determines the important social aspect of adaptation to this anthropogenic factor. The latter is based on interaction between the body with one of the most important components of the environment, earth's gravity. And, although V. A. Dekhtyarev [15] does relate development of arterial hypertension in cosmonauts to their exposure to weightlessness, we believe that other situations (forced prolonged bedrest, hypodynamia, physical fatigue, etc.) can provoke arterial hypertension. However, we agree with him entirely with regard to the fact that the "load" effect of earth's gravity must be taken into consideration when managing patients with vascular and cardiac pathology.

The above data [2, 4, 7-10] indicate that orthostatic factors intensify significantly the reactivity of hypertensive regulatory mechanisms. Under the influence of a number of factors that have a synergistic effect on antigravity reactions (for example, psychoemotional stress), pressor reactions may become more intense, while the CVS-regulating mechanisms may reach a peak level of function with subsequent change to essential hypertension.

There are data [16] to the effect that psychoemotional stress and orthostasis (the latter somewhat more so) in healthy subjects and victims of arterial hypertension lead to increase in blood renin and angiotensin levels. However, the combined effect of these factors on healthy subjects and, particularly, hypertensive ones causes a 2-fold increase in levels in blood of these biologically active substances, which trigger the most important humoral mechanism of maintaining the vascular pressor reaction.

In the opinion of K. V. Sudakov [17], development of persistent arterial hypertension on the basis of emotional stress depends on genetic and individually acquired predisposition and resistance of neuroendocrine mechanisms of individuals. We believe that the set of antigravity reactions, formed through evolution and fixed by ontogenesis, is such a genetic basis, primarily for erect-walking man. It should be noted that the functional range of these reactions includes not only hyperreactive, but hyporeactive states of the CVS.

Of course, expression of such species-specific inherited predisposition is largely determined by social and sociohygienic factors in an individual's life, in addition to biological distinctions (constitution, reactivity of CVS and hemodynamics-related systems of neuroendocrine regulation, etc.). We are referring here to the increase in exposure to the orthostatic factor, which is related to work performance and living conditions of modern man.

The progressive elevation of blood pressure of monkeys submitted to orthograde factors and walking erect is actually a manifestation of the animals' adjustment to the increased influence of earth's gravity on hemodynamics. In erect-walking beings, arterial hypertension and, apparently, hypotension constitute disturbances in the mechanism of normotensive adaptation and change to adaptation of a pathological property.

Determination of the dependence of arterial hemodynamics on properties of the functional antigravity system and state of its different regulatory elements is, in our opinion, a promising direction of research on pathogenesis of essential hypertension and hypotensive states, and it would make some contribution not only to gravity biology and physiology, but physiology and pathology of anthropogenesis.

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UDC: 629.78:612.1-06:612.766

EFFECT OF DIHYDROERGOTAMINE ON HUMAN CIRCULATION DURING ORTHOSTATIC TESTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 3, May-Jun 84 (manuscript received 22 Feb 83) pp 19-23

[Article by A. Yu. Modin, S. V. Abrosimov, O. D. Anashkin, V. V. Zhidkov, V. I. Lobachik, L. B. Parshin and V. S. Shashkov]

[English abstract from source] The physiological effects of zero-g were simulated by 6-hour antiorthostatic hypokinesia at -15°, using eight healthy volunteers. They took part in two experimental runs at a 2 week interval. During the first study the test subjects received a placebo and during the second study they got 6 mg dihydroergotamine methane sulfonate per os. Radiometric examinations of the whole body and its compartments (head, chest, abdomen legs) showed that the drug increased blood pooling in the upper body and decreased it in the lower body at every position of the long axis of the body relative to the gravity vector.

[Text] It is known that orthostatic factors cause shifting of blood into capacitive vessels of the lower half of the body and, consequently, it is more difficult for venous blood to return to the heart and cerebral vessels. During spaceflgihts, blood shifts to the upper half of the body, altering appreciably circulatory conditions. The body's adaptation to new conditions causes several substantial functional changes in hemodynamics, body fluids, hormonal regulation, etc. Such changes create additional conditions for lowering man's postural stability when he returns to earth's gravity.

One of the means of preventing orthostatic instability is to prevent gravitational deposition of blood in the veins of the lower half of the body in order to assure return of venous blood to the heart and preserve adequate delivery of blood to the brain and myocardium. Antigravity suits and elastic garments are used for this purpose [1-3]. Thus far, no effort had been made in space medicine practice to solve this problem by means of pharmacological agents. that reduce the capacity of the venous system.

Since we had information to the effect that dihydroergotamine (DHE), an ergot alkaloid, has a tonic effect on veins [4-6], we tried to assess the effect of this agent on the nature of distribution of circulating blood during postural tests and on orthostatic stability of man.

Methods

Two series of studies (with at least 14-day interval between them) were conducted in a hospital with the participation of 8 essentially healthy men 30-39 years of age. According to preliminary observations, the entire group of subjects was divided into two groups, with 4 men in each. The first group consisted of individuals with good orthostatic stability and the second those who periodically presented symptoms of orthostatic hypotension.

In the first series of studies (control), all subjects were given a placebo 30 min prior to antiorthostatic hypokinesia (AOH) and in its 3d and 5th hours. In the second series, they took 2 mg DHE (dihydroergotamine methanesulfonate) by mouth. Total dosage of this agent was 6 mg.

The physiological effects of weightlessness were simulated by 6-h AOH at a tilt angle of -15°. To test orthostatic stability, we ran a 20-min passive orthostatic test at a 75° angle immediately after AOH.

The EKG was taken continuously to monitor heart rate (HR). Arterial pressure (BP) was measured discretely with an automatic gage. Redistribution of circulating blood during the orthostatic test was determined on a special stand, the operating principle of which was based on simultaneous radiometry of the whole body and its parts (head, chest, abdomen and lower limbs), followed by computer processing and output of results as percentage of circulating blood volume (CBV) in different parts of the body. We used ^{113m}In in a dosage of 0.26 Bq/kg weight as a radiotracer. Circulating plasma volume (CPV) was determined on the basis of dilution of ^{131}I-albumin of human serum, which was injected intravenously in a dosage of 0.18-0.36 mBq. CBV was found using the following formula:

$$CBV = \frac{CPV \cdot 100}{100 - H \cdot 0.9}$$

where H is hematocrit of venous blood and 0.9 is the coefficient for calculating total-body hematocrit [7]. Venous blood hematocrit was assayed on a microhematocrit centrifuge at 8000 r/min for 5 min.

The volume of blood drawn for the radiometric studies was replaced with isotonic sodium chloride solution.

The results were submitted to statistical processing by the method of variants related in pairs.

Results and Discussion

The first group of subjects tolerated well the orthostatic tests in both series. Two of the subjects in the second group presented a collaptoid reaction in the first series and four did so in the second.

The results listed in Table 1 indicate that, under the influence of DHE, the subjects in the first group showed some improvement of orthostatic stability, as compared to control values. In spite of the insignificant decrease in CBV, these subjects presented less marked HR increase and decline of pulse pressure during the orthostatic test. Systolic BP rose during orthostatic tests.

Table 1. HR, BP, CBV and CPV before and during orthostatic test (n = 4)

Indicator	Series I		Series II	
	group			
	1	2	1	2
HR/min:				
mean before orthostatic test	69	57	65	57
maximum during orth. test	103	101	95*	101
BP before orth. test				
systolic	131	129	132	129
diastolic	81	76	83	72
pulse	50	53	49	57
BP during orth. test				
systolic	124	122	136*	130
diastolic	89	80	91	91*
pulse	35	42	45	39
CBV, ml/kg weight:				
before orth. test	75,6	75,9	73,4	66,7
10th min of orth. test	78,0	—	74,5	—
20th min of orth. test	71,5	—	69,4	—
CPV, ml/kg weight:				
before orth. test	42,6	45,5	42,1	39,8
10th min of orth. test	42,6	—	40,5	—
20th min of orth. test	39,5	—	38,1	—

* $P \leq 0,05$.

As noted above, orthostatic stability worsened with intake of DHE in the second group of subjects. This was apparently attributable to appreciable decrease of CBV (to 17%, as compared to control data) in 3 cases, while the fourth subject had a CBV that was somewhat greater than the control level before the orthostatic test and this explains development of collaptoid reaction in the 13th min in this subject, rather than the 4th as in the control series.

As shown in Table 2, there was change in nature of blood distribution under the effect of DHE, both in head-down and horizontal positions, as well as erect. For subjects in both groups, this was manifested by greater delivery of blood to the upper part of the body and less blood in the bottom part. At the same time, during the orthostatic test in the second series of studies, all subjects showed increased efflux of blood from the head; there was no associated decrease in filling of organs in the chest. Interestingly, there was increased shifting of blood to capacitive vessels of the abdomen in all subjects who took DHE, and in the first group this shift was demonstrated mainly in the first minutes of the test, with subsequent stabilization of the process. In the second group of subjects, during the orthostatic test the increase in filling with blood of the abdomen continued to progress and reached a maximum prior to development of collapse. Gravity-related shifting of blood to the lower extremities was less marked in the 1st min of the orthostatic test with intake of DHE, whereas in

the 10th and 20th min it was more marked than in the control study. In spite of this, total blood volume was smaller in the second series than the first throughout the test period.

Table 2. Distribution of blood (in % CBV) in different parts of the body with subjects (n = 4) in different positions

Position	Part of body	I		II	
		group			
		1	2	1	2
Head-down tilt	Head	11,88	11,04	12,98*	12,21*
	Chest	37,41	40,13	39,66	42,45**
	Abdomen	32,92	29,78	30,44	27,26
	Legs	17,70	18,96	16,78	17,98*
Horizontal	Head	11,24	10,19	12,13*	11,63
	Chest	35,62	36,98	37,57	39,80**
	Abdomen	33,23	32,31	31,74	28,55
	Legs	19,73	20,43	18,47*	19,91
Orthostatic, 1st min of test	Head	10,10	9,35	10,12	10,05
	Chest	27,62	26,02	29,45*	28,60**
	Abdomen	35,10	34,88	34,91	32,84
	Legs	27,17	29,67	25,45*	28,47
Same, 10th min of test	Head	9,62	—	9,62	—
	Chest	24,80	—	26,70	—
	Abdomen	34,27	—	33,00	—
	Legs	31,20	—	30,60	—
Same, 20th min of test	Head	9,47	—	9,48	—
	Chest	24,62	—	26,40*	—
	Abdomen	34,70	—	33,32	—
	Legs	31,12	—	30,70	—

* $P<0,05$
** $P<0,01$

Measurement of CPV before and in the 20th min of the orthostatic test revealed a reliable ($P<0.05$) decrease in plasma volume in the vascular system of the 1st group of subjects by 7% in the first series and 10% in the second. Unfortunately it was impossible to obtain information about CPV changes in the 2d group of subjects during the orthostatic test due to their development of collaptoid reactions and discontinuation of the studies.

The decrease in CPV during the orthostatic test is viewed as the result of plasma filtration from vessels of the lower limbs to the perivascular space under the influence of increased hydrostatic blood pressure in this region during the orthostatic tests [8]. In our studies, we were impressed by the fact that, while there was a somewhat low hydrostatic pressure (insignificant decline of CBV in the second series of studies in subjects of the 1st grup), filtration plasma loss was more marked with intake of DHE than in the control. This warrants the assumption that DHE creates conditions for increased filtration of the liquid part of blood into the interstitial space. The possibility cannot be ruled out that such a phenomenon could also occur in the 2d group of subjects, worsening orthostatic instability, along with the hypovolemia factor.

Since fluid intake was not recorded in our studies, while measurement of CPV and CBV before AOH and diuresis during AOH was not made, we cannot determine whether the CBV decline in the 2d series is related to DHE intake on the basis of existing CPV and CBV levels.

A positive answer to this question may be given by the relatively greater blood content of chest organs during AOH with intake of DHE. There are reports of proportionate values for intrathoracic blood volume and intensity of fluid loss [9].

Thus, we did not obtain unequivocal information about the effect of DHE on orthostatic resistance of man. With respect to prevention of orthostatic instability, we observed both positive and negative aspects of DHE pharmacodynamics. The relative increase in blood content in the system of intrathoracic vessels during orthostatic tests under the effect of DHE unquestionably merits a positive rating. The relative increase in delivery of blood to the head and chest organs in antiorthostatic and horizontal positions, as well as more marked postural efflux of blood from the head are the negative aspects of DHE effect. If the suspected link between intake of DHE and increased diuresis is confirmed, there will be serious obstacles to future consideration of this agent as a potential means of preventing orthostatic instability. The increase we observed in filtration of liquid part of blood into perivascular tissues under orthostatic conditions with intake of DHE requires experimental confirmation, in view of the small number of cases (4). The physiological consequences of the possible α-adrenolytic effect of DHE, though it is not inherent in the dosage we used, should also be viewed as potential limitations to the preventive value of this agent.

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CIRCULATORY CHANGES IN ORTHOSTATIC POSITION IN THE PRESENCE OF HYPERTHERMIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 3, May-Jun 84 (manuscript received 30 Mar 83) pp 23-25

[Article by V. I. Sobolevskiy and V. P. Pravosudov]

[English abstract from source] It has been shown that orthostatic tolerance does not deteriorate if the level of hyperthermia and weight losses are controlled. Orthostatic intolerance develops at a critical level of hyperthermia and water losses. The mechanisms of this effect are described. The results obtained can be used to improve the aerospace expertise quality.

[Text] Investigation of distinctions of orthostatic circulatory reactions under different conditions of vital function, in particular in the presence of exogenous hyperthermia, is an urgent problem of aerospace medicine [1, 2]. The few studies of orthostatic tolerance with exposure to high temperatures [3] do not shed light on many physiological aspects of this problem. Moreover, since some of the effects of hyperthermia (change in blood pressure--BP, circulating blood volume and peripheral resistance) are deciding factors in the response to orthostatic conditions, it is interesting to investigate the circulatory changes in orthostatic position as related to different degrees of overheating.

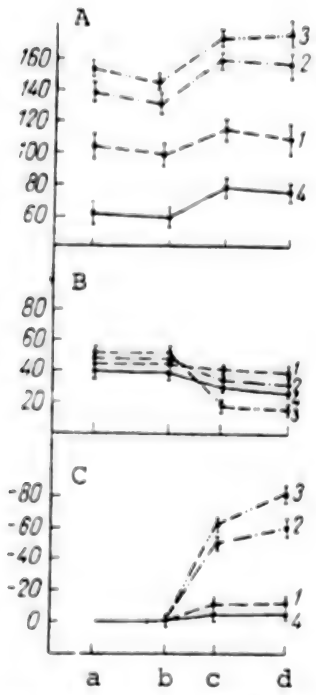
Methods

A total of 46 essentially healthy men, 19-37 years of age, participated in these studies; they were divided into 3 groups in accordance with heat exposure. Exogenous hyperthermia was produced in a sauna (air temperature 90°C, relative humidity 10-15%). Subjects exposed to heat for 10 min made up the 1st group (n = 16), those exposed for 15 min made up the 2d group (n = 16) and for 20 min, the 3d group (n = 14); no contrast cooling was used. The control consisted of 20 men who made up the 4th group. We measured sublingual temperature (T_S), BP and recorded the EKG in the 12 convential leads and Neba leads, as well as fluid loss by weighing, in all subjects. The test was conducted with the subjects in horizontal position, then in erect position in the 1st, 3d and 5th min, before and after exposure to heat in a room with ambient temperature of 24.4± 0.5°C.

Results and Discussion

Both base values and those obtained during orthostatic tests for pulse, BP and EKG showed no reliable differences before exposure to heat in all groups of subjects.

During hyperthermia, the orthostatic circulatory reactions changed appreciably, there being a reliable correlation (see Table) between orthostatic tolerance and several indicators of heat regulation; this correlation increased with increase in body temperature. T_s rose to a mean of 37.6±0.2°C, heart rate (HR) increased to 101.4±7.7/min and weight loss constituted 0.31±0.09% of base value in the first group of subjects. Systolic BP rose by 4.3±0.1 and diastolic BP dropped by 8.1±0.8 mm Hg. The EKG showed changes that have been previously described, which were indicative of physiological nature of adaptive myocardial reactions to hyperthermia [5]. During the orthostatic test (see Figure), with hyperthermia the HR increment did not differ reliably in the 1st and 4th groups, whereas in the 5th min of the orthostatic test BP of the 1st group of subjects dropped to base level and in the 4th group dropped by 3.9 mm Hg; diastolic BP rose in both groups, and it reached base values in the 1st group of subjects. Such BP dynamics are indicative of stabilization of pulse pressure during the orthostatic tests in the presence of moderate hyperthermia. The EKG showed adaptive changes that did not exceed the normal range, although one subject developed signs of impaired repolarization of cardiac ventricles (T/R < 10%) in erect position, without worsening of general well-being.



Changes in HR (A), pulse pressure (B) and decline of T wave on EKG (C) during orthostatic test before and during hyperthermia
a, b) supine position, 1st and 5th min, respectively
c, d) erect, 1st and 5th min
1-3) 1st-3d groups
4) 4th group

In the 2d group of subjects, T_s rose to 38.4±0.2°C, weight loss constituted 1.8±0.4% of base value, HR reached 139.7±11.3/min, systolic BP rose by 4.9 mm Hg and diastolic dropped by 6.2±1.1 mm Hg. In 25% of the cases, the EKG showed a substantial decrease in amplitude of T wave, oblique decline of ST segment below the isoline with increase in following function:

$$\frac{Q - X}{Q - T} > 50\%$$

By the 5th min of the orthostatic test (see Figure) the HR increment was reliably greater than in the control group, systolic BP dropped and diastolic pressure showed virtually no change. The EKG showed flattening of T wave to the isoline (in 43.8% of the subjects), excessive decline of ST segment below the isoline according to Q - X/Q - T > 50% criterion

(in 12.5% of the subjects). The EKG of one subject showed ventricular extrasystole and two developed a presyncopic state.

Correlation between indicators of heat regulation and orthostatic tolerance

Indicator of heat regulation	Group	Pulse increment, per min	Change in pulse pressure, mm Hg	Decline of T wave on EKG, % of base value
Sublingual temperature, °C	1	0,602	—0,412	0,732
	2	0,621	—0,429	0,768
	3	0,712	—0,493	0,796
Weight loss, % of base value	1	0,681	—0,539	0,785
	2	0,696	—0,539	0,789
	3	0,747	—0,616	0,804

Note: This table lists the dynamics of correlation coefficient r according to Spearman.

In the 3d group of subjects, T_s rose to a mean of 39.2±0.3°C, weight loss constituted 2.2±0.3% of base value, HR reached 147.8±11.3/min, systolic BP did not change and diastolic pressure was 2.4±0.4 mm Hg lower than the base level. The EKG of 57.1% of the subjects showed marked signs of impaired cardiac function (decline or inversion of T wave, atrioventricular grade I block, increase by more than 0.04 s in electrical systole, as compared to nominal value). Orthostasis (see Figure) elicited a substantial change in circulation, which was pathological in 85.7% of the subjects, which was indicative of breakdown of circulatory compensatory mechanisms; by the 5th min of orthostatic testing, systolic pressure dropped by 18.9 mm Hg, diastolic BP rose by 9.8 mm Hg, the EKG showed aggravation of existing functional disturbances of the heart and there was appearance of ventricular extrasystole. A syncopic state developed in four subjects.

It is known that moderate hyperthermia causes increase in circulating blood volume, improves coronary circulation and regulation of vascular tonus, which leads to elevation of central venous pressure and increased cardiac output [5-7], and has a beneficial inotropic effect [5]. At the same time, these factors determine the dynamics of orthostatic stability [1, 5, 9] which, according to the results of this investigation, did not differ reliably, with T_s up to 37.6±0.2°C and weight loss of up to 0.31±0.09%. A greater degree of hyperthermia (≥38.4°C), which elicits thermal hypoxia in the body [1, 6, 11] and leads to cardiac hyperfunction [8], causes considerable functional disturbances in the heart due to transient hypoxia, which develops during orthostatic tests [10]. In addition, heat dehydration and loss of sodium salt with perspiration could cause decline of tissue pressure and, consequently, increase deposition of blood in veins of the feet [11], which provokes development of syncopic states during orthostatic tests, against the background of thermogenic decrease in peripheral resistance [6] and worsening of cardiac function. Several authors [12] failed to demonstrate changes in circulatory reaction to orthostatic factors, with fluid loss of up to 3% of body weight. However, in our studies, there was a reliable correlation between indicators of dehydration and

orthostatic tolerance in the case of overheating, which confirms the assumption [2] that the extent of fluid loss is a potential factor of change in orthostatic stability.

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BLOOD PLASMA FREE AMINO ACIDS UNDER HYPOKINETIC CONDITIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 3, May-Jun 84 (manuscript received 18 Mar 83) pp 25-34

[Article by I. G. Popov and A. A. Latskevich]

[English abstract from source] The study (in a Hitachi KLA-3B analyzer) of 17 free amino acids in plasma of six healthy men under ambulatory and hypokinetic conditions demonstrated the following trend: by day 15 of clinostatic hypokinesia the content of most amino acids increased and by day 30 decreased, reaching the pretest level or falling below it. These variations in the amino acid concentration are viewed as a consequence of the modified relations between anabolic and catabolic processes induced by adaptation to hypokinesia. It is emphasized that the nutrition pattern was different in the hypokinetic study.

[Text] Hypokinesia is one of the constant factors in the habitat of spacecraft. The change from the ground-based mode of life, with rather high physical loads during the period of preflight training, to conditions of limited motor activity in the compartments of spacecraft must be associated with change in quantitative and qualitative characteristics of metabolism in cosmonauts. Indeed, a number of changes in different forms of metabolism under the effect of the set of spaceflight factors are due, to some extent, to the influence of hypokinesia and change to a mode of life involving lighter physical loads. Some authors emphasize in particular the changes in nitrogen and protein metabolism during spaceflights [1-3]. For this reason, it is interesting to study the metabolism of amino acids, which hold a key position in processes of protein metabolism and are directly involved in nitrogen metabolism, in order to understand the biochemical processes that take place under the influence of spaceflight factors, including hypokinesia.

There are few reports in the literature concerning the distinctions of amino acid metabolism as related to diminished physical activity and strict hypokinesia [4-8]. Some of these studies were conducted on animals [4-6], others [7-8] were conducted under different hypokinetic conditions or else did not contain details about the dynamics of the entire spectrum of amino acids, diet of the subjects, analysis of initial amino acid status, dynamics of the pool of amino acids under hypokinetic conditions in the recovery period.

We submit here the results of assaying 17 free amino acids of blood plasma before submitting the tested subjects to hypokinesia and during the 30 days of strict clinostatic hypokinesia.

Methods

This study was conducted on six male volunteers 18-23 years of age, who were deemed to be in essentially good health after a clinical examination and suitable for flight tests. Before being submitted to hypokinesia, they spent more than 3 months under ordinary conditions with physical loads constituting 3000-3400 kcal/day expenditure of energy. They were all on the same diet: about 100 g protein, 150 g fat, 400 g carbohydrate, for a total of 3350 kcal/day (assimilable). During the test period, in order to assure strict hypokinetic conditions, all of the subjects spend 30 days on continuous bedrest in horizontal position (clinostatic hypokinesia). During the hypokinetic period, the subjects received a standard food allowance: 92-111 g protein, 125-138 g fat, 296-315 g carbohydrates, with a total of 2677-2946 kcal/day. They were given a multiple vitamin. It was one of the variants of the Aerovit food allowance for the crew of Salyut-3 spacecraft.

We assayed 17 free amino acids in samples of venous blood, which was drawn in the morning, on a fasting stomach. A standard method was used to prepare the specimens of blood and plasma [9-12]. Amino acids were assayed using the Hitachi automatic amino acid analyzer (model KLA-3B).

The obtained concentrations of amino acids were compared for different times and to the findings of other authors [7, 8, 12-18, 21], as well as to our own data obtained from tests on cosmonauts [11, 24] and healthy men under ordinary living conditions.

Results and Discussion

Table 1 lists the concentrations of 17 free amino acids in the subjects' blood plasma before 30-day clinostatic hypokinesia under ordinary living conditions and on their usual diet; it also lists the data of other authors, which they recommend as the physiological "norm" for healthy adults. In the right part of Table 1 are the data we obtained from a study of 124 adult men under ordinary living conditions in a temperate climate, while engaged in their professional activity, which was characterized by light to moderately heavy physical loads (professional groups I and II for physiological dietary norms of the USSR Academy of Medical Sciences--1968), on an ordinary diet that was not regulated.

Let us compare the concentrations of free amino acids that we found to the "norms" proposed by other authors and to our findings in a survey of adult men under ordinary living and dietary conditions.

According to the "approximate data for adults" listed in the literature [18], the levels of most plasma amino acids were in the range of their physiological fluctuations when our subjects were under ordinary living conditions. The only exception was aspartic acid, the concentration of which was much lower in the subjects than the bottom of the range of physiological fluctuations. It should also be noted that some subjects showed a methionine concentration close to the bottom limit, while lysine and glutamic acid were close to the top of the physiological range of these amino acids.

Table 1. Blood plasma free amino acid levels under ordinary living conditions before hypokinesia in our subjects, as well as healthy adults under various living conditions according to data of other authors (mg%)

AMINO ACID	OUR SUBJECTS UNDER ORDINARY CONDIT (n=6)	DATA IN THE LITERATURE							OUR 1982 DATA (124 HEALTHY MALES)
		[12, 13]	[14, 15]	[16]	[17]	[18]	[7, 20, 21]	[19]	
ALANINE	2,86 ± 0,19	3,41	3,01 — 3,73	3,2 — 5,6	3,07 (2,22 — 4,47)	3,0 (2,0 — 4,0)	3,8 ± 0,14	3,4	2,84 ± 0,04
ARGININE	1,45 ± 0,17	1,51	1,22 — 1,93	1,6 — 3,0	1,43 (0,86 — 2,63)	2,0 (1,0 — 3,0)	1,07 ± 0,08	1,62	1,33 ± 0,02
ASPARTIC ACID	0,32 ± 0,04	0,03	0,01 — 0,07	—	0,22 (след. — 0,72)	3,5 (2,0 — 5,0)	0,7 ± 0,05	0,03	0,29 ± 0,07
VALINE	2,41 ± 0,15	2,88	2,37 — 3,71	2,2 — 3,2	1,99 (1,36 — 2,66)	2,25 (1,5 — 3,0)	2,54 ± 0,06	2,88	2,33 ± 0,02
HISTIDINE	1,65 ± 0,20	1,15	0,79 — 1,48	1,7 — 2,1	1,24 (0,97 — 1,45)	1,4 (0,8 — 2,0)	1,64 ± 0,08	1,38	1,12 ± 0,01
GLYCINE	1,60 ± 0,06	1,54	1,34 — 1,73	2,8 — 3,0	1,74 (1,08 — 3,66)	2,5 (1,0 — 4,0)	2,32 ± 0,09	1,5	1,46 ± 0,02
GLUTAMIC ACID	3,79 ± 0,25	0,70	0,43 — 1,15	0,8 — 1,1	0,86 (0,25 — 1,73)	2,35 (0,7 — 4,0)	3,97 ± 0,26	0,70	4,13 ± 0,05
ISOLEUCINE	0,98 ± 0,04	0,89	0,69 — 1,28	1,6 — 2,0	0,71 (0,46 — 1,15)	0,75 (0,5 — 1,0)	1,05 ± 0,05	1,34	0,82 ± 0,01
LEUCINE	1,88 ± 0,08	1,69	1,42 — 2,3	1,7 — 3,2	1,32 (0,93 — 1,78)	2,00 (1,0 — 3,0)	2,03 ± 0,08	1,86	1,60 ± 0,02
LYSINE	3,93 ± 0,43	2,72	2,61 — 3,02	2,1 — 5	2,54 (2,11 — 3,09)	2,5 (1,0 — 4,0)	3,22 ± 0,15	2,72	3,65 ± 0,06
METHIONINE	0,41 ± 0,03	0,38	0,33 — 0,43	0,3 — 0	0,32 (0,23 — 0,39)	0,5 (0,3 — 0,7)	0,54 ± 0,04	0,52	0,33 ± 0,00
PROLINE	2,32 ± 0,11	2,36	2,01 — 3,34	2,6	2,71 (1,28 — 5,14)	1,75 (0,5 — 3,0)	2,76 ± 0,08	2,36	2,25 ± 0,02
SERINE	1,76 ± 0,13	1,12	1,01 — 1,25	1,16	1,18 (0,68 — 2,03)	1,5 (1,0 — 2,0)	2,02 ± 0,09	1,12	1,51 ± 0,02
TYROSINE	0,99 ± 0,07	1,03	0,81 — 1,45	1,4 — 1,5	0,91 (0,65 — 1,13)	1,3 (0,6 — 2,0)	1,04 ± 0,06	1,04	0,92 ± 0,01
THREONINE	2,06 ± 0,23	1,39	1,21 — 1,72	1,9 — 2,1	1,94 (1,22 — 2,93)*	2,0 (1,0 — 3,0)	1,91 ± 0,09	1,67	1,94 ± 0,04
PHENYLALANINE	0,92 ± 0,05	0,84	0,69 — 0,95	1,4 — 1,9	0,95 (0,63 — 1,92)*	1,25 (0,5 — 2,0)	1,13 ± 0,06		0,88 ± 0,01
CYSTINE	0,77 ± 0,05	1,18*	1,08 — 1,3*	2,0 — 3,0	1,77 (1,15 — 3,37)	2,00 (1,0 — 3,0)**	0,91 ± 0,10	1,47*	0,75 ± 0,01

*Cystine + cysteine

**Cysteine

Table 2. Overall indicators of levels of 17 free amino acids in subjects' blood plasma under ordinary living conditions, as well as on 15th and 30th days of hypokinesia (mg%)

OVERALL INDICATORS OF STATUS OF AMINO ACID POOL OF BLOOD PLASMA	OUR SUBJECTS UNDER ORDINARY CONDI-TIONS (n=6)	DATA IN THE LITERATURE							OUR DATA (124 HEALTHY MEN)	OUR SUBJECTS DURING HYPOKINESIA	
		[12, 13]	[14, 15]	[16]	[17]	[18]	[7, 20, 21]	[9]		15TH DAY (n=6)	30TH DAY (n=6)
TOTAL ESSENTIAL AMINO ACIDS (E)	12,59 ± 0,52	10,79	9,22 — 13,41	11,2 — 18,3	9,77 (6,94 — 13,92)	5,8 — 16,7	12,42 + 0,22	10,99*	11,55 ± 0,06	12,34 ± 0,47	12,16 ± 0,36
TOTAL NON-ESSENTIAL AMINO ACIDS (NE)	17,51 ± 0,46	14,03**	11,71 ± 17,43**	17,26 — 23,06	15,13 (9,14 — 26,33)	10,6 — 32	10,23 ± 0,37	14,62*	16,60 ± 0,01	18,34 ± 0,43	18,50 ± 0,41
TOTAL FREE AMINO ACIDS (E+NE)	30,10 ± 0,69	24,82**	20,93 — 30,84**	28,46 — 41,36	24,9 (16,08 — 40,25)	16,4 — 48,7	32,65 ± 0,43	25,61*	28,15 ± 0,06	31,68 ± 0,64	30,60 ± 0,52
E/NE RATIO	0,72 ± 0,03	0,77	0,79 — 0,77	0,64 — 0,79	0,66 (0,75 — 0,52)	0,54 — 0,52	0,61 ± 0,01	0,75	0,69 ± 0,03	0,73 ± 0,03	0,65 ± 0,02

*Without phenylalanine

**Cystine + cysteine

A comparison of amino acid levels in the subjects' plasma to the "norms" recommended by B. I. Zbarskiy et al. [16], which are used extensively at the present time in clinical practice, yielded different results. According to these norms, concentrations of valine, lysine, methionine, arginine, histidine, leucine and threonine were in the range of physiological fluctuations in the subjects. The concentrations of arginine, histidine and leucine were close to the bottom of the range, while that of threonine was close to the top of the range of physiological fluctuations. Concentrations of alanine, glycine, isoleucine, proline, tyrosine, phenylalanine and cystine were lower in the subjects than normal levels, while glutamic acid and serine were higher than normal.

As compared to the physiological "norm" cited by Muller in his manual of clinical biochemistry [17], the levels of most amino acids in the plasma of our subjects were in the range of their physiological fluctuations in healthy adult men. In all of the subjects, only the concentration of cystine was lower than the bottom of the "normal" range. Plasma lysine, leucine and glutamic acid levels exceeded the top of the physiological range in all of the subjects, while some of them presented such high levels for tyrosine and histidine.

According to the average concentrations of blood plasma amino acids given in the well-known textbooks by N. N. Pushkina [13] and N. V. Semenov [15], on the basis of the standards proposed by Moore and Stein [12] and Dimmer [14], the concentrations of most amino acids in the subjects were in the range of physiological fluctuations and in some cases even above the top of the "normal" range. This applies to lysine, threonine, aspartic and glutamic acids, histidine and serine. Only the concentration of alanine and valine was low in some subjects. It is difficult to draw a conclusion about cystine, since the above-mentioned authors cited a combined value (cystine + cysteine).

The average concentrations of blood plasma amino acids cited by I. B. Zbarskiy [19] were close to the findings on our subjects for arginine, histidine, glycine, leucine, proline and tyrosine, but they are higher for alanine, valine, isoleucine and methionine. In our subjects, aspartic and glutamic acid, lysine, serine and threonine content was above the mean values cited by the above author. The mean concentrations of blood plasma amino acids obtained by A. S. Ushakov and T. F. Vlasova [7, 20, 21] using equipment similar to ours were very close to the data obtained on our subjects with regard to valine, histidine, glutamic acid, isoleucine, leucine, lysine, methionine, tyrosine, threonine, phenylalanine and cystine. But plasma alanine, aspartic acid, glycine, proline and serine levels in our subjects were lower than the norm indicated by the above authors, while arginine level was higher than theirs.

If we compare our data listed in Table 1 and those obtained with the same equipment for 124 healthy men, also under ordinary living conditions, it is not difficult to become convinced that the concentrations of most amino acids in the 6 subjects examined were within the range of average values for our "norm" before hypokinesia. It is only with regard to histidine, isoleucine, leucine, methionine and serine that one can conclude that their concentrations in the subjects were somewhat above average values that we obtained previously in a study of the other 124 people.

Analysis of data obtained on the subjects before hypokinesia enables us to draw the following conclusion.

Under ordinary living conditions, the concentrations of most free amino acids in plasma of our subjects were in the physiological range inherent in healthy adults, as compared to the physiological "norms" of any of the above-mentioned authors [12-19]. This applied the most when we compared amino acid concentrations of the subjects to values that we had previously established, as well as those of A. S. Ushakov and T. F. Vlasova [7, 20, 21]. At the same time, it should be noted that, under ordinary living conditions, the subjects demonstrated low levels of aspartic acid [18], alanine, glycine, isoleucine, proline, tyrosine, phenylalanine and cystine [16], cystine, alanine and valine in some individuals [12-15], alanine, aspartic acid, glycine, proline and serine [7, 20, 21]. In our subjects, the concentrations of the following exceeded the top of the "normal" range: glutamic acid and serine [16], methionine, tyrosine and histidine in some cases [1-7], lysine, threonine, aspartic and glutamic acids, histidine and serine [12-15], arginine [7, 20, 21], histidine, isoleucine, leucine, methionine and serine, as compared to our data for 124 other men under ordinary living conditions.

The overall indicators of plasma amino acid levels in subjects under ordinary conditions are listed in Table 2. Most of the cited authors give the concentrations of only some amino acids, so that the overall indicators listed in Table 2 are the result of our statistical processing of data listed in Table 1.

The sum of essential amino acids (E) in the subjects was close to the value given in the literature [7, 20, 21] and the indicator we obtained in a study of 124 other healthy adults. According to the data of other authors, this parameter was in the range of physiological fluctuations in our subjects. A lower value cited by I. B. Zbarskiy [19] is attributable to the fact that it represents the sum of 16, rather than 17, amino acids (without phenylalanine).

Total nonessential amino acids (NE) were also close to the average for this parameter that we obtained in a study of 124 people under ordinary conditions, and within the physiological range calculated on the basis of data of other authors. Some authors cite a higher value for this indicator [7, 20, 21] and others, a lower one [12, 13, 17, 19]. We can also mention some tendency toward increase of the parameter for NE in the subjects, as compared to our mean values.

The sum of blood plasma amino acids (E + NE) in the subjects was in the range of physiological fluctuations [12, 13, 17, 20, 21]. A comparison to the mean values given by other authors revealed that this overall indicator for the subjects either exceeded theirs [12, 13, 17] or was lower [20, 21]. Our study of 124 other people yielded a mean value that was lower than in the subjects prior to hypokinesia.

The E/NE ratio in blood plasma of the subjects was quite close to the value obtained from processing the data of most of the cited authors. Lower values were obtained according to the data of some authors [7, 17, 18, 20, 21], as well as in our testing of 124 other people.

Our analysis leads us to conclude that individuals under ordinary living conditions with different working, recreation, diet, etc., conditions show some differences both in concentrations of different amino acids and in total essential and nonessential amino acids, as well as the ratio between them.

All this makes it urgent to further develop the physiological norms for levels of blood plasma amino acids that are differentiated according to living conditions and diet. It would be desirable to have such standards, along with more general physiological norms for healthy adults.

According to the concentrations of amino acids listed in Table 3, on the 15th day of hypokinesia there was virtually no change in arginine, glutamic acid, isoleucine and tyrosine levels in the subjects' blood plasma, since the demonstrated differences from base values do not exceed 2%, which is consistent with accuracy of the method. The concentrations of alanine, aspartic acid, valine, glycine, leucine, lysine, proline, serine, threonine and phenylalanine increased on the 15th day of hypokinesia. The following showed the greatest increase: alanine (by 21.7%), aspartic acid (15.6%), threonine (11.2%), valine and phenylalanine (8.7%). However, the increase in concentration was reliable only for alanine. At the same time, plasma levels of histidine, methionine and cystine dropped on the 15th day of hypokinesia, particularly cystine (by 10.4%) and methionine (by 7.7%).

Table 3. Blood plasma free amino acid levels (mg%) in subjects under hypokinetic conditions (n = 6).

AMINO ACID	ORDINARY LIVING CONDIT. AND DIET (BASE PERIOD) M±m	CLINOSTATIC HYPOKINESIA ON DIET INCLUDING PRESERVED AND CONCENTRATED FOODS						CHANGE IN AMINO ACID CONTENT ON 30TH DAY AS COMPARED TO 15TH DAY, %
		15TH DAY OF HYPOKIN.			30TH DAY OF HYPOKIN.			
		M±m	CHANGE IN M AS COMPARED TO BASE VALUE		M±m	CHANGE IN M AS COMPARED TO BASE VALUE		
			MG%	%		MG%	%	
ALANINE	2,86±0,19	3,48±0,19*	+0,62	+21,7	3,40±0,22	+0,54	+18,9	−2,3
ARGININE	1,45±0,17	1,48±0,12	+0,03	+2,1	1,67±0,09	+0,22	+15,2	+12,8
ASPARTIC ACID	0,32±0,04	0,37±0,04	+0,05	+15,6	0,35±0,02	+0,03	+9,4	−5,4
VALINE	2,41±0,15	2,62±0,13	+0,21	+8,7	2,18±0,03	−0,23	−9,5	−16,8
HISTIDINE	1,65±0,20	1,58±0,13	−0,07	−4,2	1,73±0,14	+0,08	+4,8	+9,5
GLYCINE	1,60±0,06	1,72±0,14	+0,12	+7,5	1,74±0,08	+0,14	+8,8	+1,2
GLUTAMIC ACID	3,79±0,25	3,82±0,19	+0,03	+0,8	4,01±0,19	+0,22	+5,8	+4,9
ISOLEUCINE	0,98±0,04	0,99±0,04	+0,01	+0,1	0,79±0,01**	−0,19	−19,4	−20,2
LEUCINE	1,88±0,08	1,94±0,15	+0,03	+3,2	1,67±0,03	−0,21	−11,1	−13,9
LYSINE	3,93±0,43	4,12±0,36	+0,19	+4,8	4,09±0,21	+0,16	+4,1	−0,7
METHIONINE	0,41±0,03	0,38±0,02	−0,03	−7,7	0,35±0,03	−0,06	−14,6	−67,9
PROLINE	2,32±0,11	2,41±0,20	+0,09	+3,9	2,30±0,06	−0,02	−0,9	−4,6
SERINE	1,76±0,13	1,91±0,14	+0,05	+2,8	1,61±0,09	−0,15	−8,5	−11,1
TYROSINE	0,99±0,07	0,98±0,04	−0,01	−1,0	0,91±0,04	−0,08	−8,1	−7,2
THREONINE	2,06±0,23	2,29±0,22	+0,23	+11,2	2,15±0,29	+0,09	+4,4	−6,1
PHENYLALANINE	0,92±0,05	1,00±0,06	+0,08	+8,7	0,79±0,01**	−0,19	−19,4	−2,1
CYSTINE	0,77±0,05	0,69±0,08	−0,08	−19,4	0,78±0,09	+0,01	+1,3	+13,0

Note: The amino acids are listed in the same order as in the BME [Great Medical Encyclopedia], 3d edition, 1980, p 108.

*P<0.05
**P<0.01

On the whole, there is the impression that there was a tendency toward increase in concentrations of most amino acids on the 15th day of hypokinesia. This trend was the most marked for alanine, aspartic acid, threonine, valine and phenylalanine. It could be due to decreased requirement for these amino acids under conditions of strict clinostatic hypokinesia as a result of diminished intensity of anabolic processes. The blood plasma pool of free amino acids could have been replenished endogenously by release of many of them in the course of intensification of catabolic processes in muscle cells under the effect of hypokinesia. The food allowance, which had a high enough energy value for hypokinetic conditions, should have been instrumental, in turn, in increasing amino acid content of blood plasma. Of course, changes in renal and liver function could have played some part.

The dynamics of methionine, cystine and histidine levels was somewhat contradictory to the general tendency toward increase in concentrations of most amino acids. By the 15th day of hypokinesia their concentrations in blood decreased. The decrease in plasma concentration of methionine and cystine could have been due, to a significant extent, to alimentary causes. During hypokinesia, the subjects were on a diet consisting mainly of preserved products. It is known that the amino acid composition of canned meat and dairy products is limited for methionine and cystine [22]. Methionine is not synthesized in the human body. It should be noted that a decrease in plasma concentrations of expressly these amino acids was found right after termination of spaceflights, when such diets were used during missions. There may be another cause for the decrease in blood plasma histidine. There are data to the effect that the first step in the sequence of reactions of histidine synthesis is catalyzed by the regulatory enzyme, phosphoribosylpyrophosphate-ATP-phosphorylase, which is inhibited by the end product of this route, histidine. This enzymatic system is subject to coordinated repression [23]. Consequently, when there is a surplus of histidine in cells, there is repression of synthesis of all enzymes involved in its biosynthesis. For this reason, the demonstrated decrease in blood plasma histidine concentration in our subjects could have been due to decrease in its biosynthesis to a lower level that is adequate to prevailing conditions. The decrease in intensity of anabolic processes under hypokinetic conditions, which are associated with a decrease in histidine requirement and increase in its concentration in cells, should have been instrumental in diminishing histidine synthesis.

Summary indicators of 17 free amino acids in the subjects' plasma on the 15th day of hypokinesia are listed in Table 2. As compared to analogous indicators in the base period, there had been some increase in total sum of amino acids, sum of essential and nonessential amino acids (E + NE), as well as E/NE ratio by the 15th day. Since the changes were minor as a whole, we can only discuss the existence of some tendency toward increase in pool of free amino acids and pool of essential ones, as well as nonessenital amino acids, with insignificant change in ratio between them in the direction of increase (due to relatively greater increase in pool of essential amino acids).

On the 30th day of hypokinesia, only proline and cystine levels were virtually the same as under ordinary living conditions (±2%), according to their mean concentrations. Plasma levels of eight amino acids were higher than in the base period: alanine, arginine, aspartic and glutamic acids, histidine, glycine,

lysine, threonine. The following presented the most marked increase: alanine (by 18.9%), arginine (15.2%), aspartic acid (9.4%) and glycine (8.8%). There was decrease in concentrations of seven amino acids: valine, isoleucine, leucine, methionine, serine, tyrosine and phenylalanine. The most marked declines were referable to isoleucine and phenylalanine (by 19.4%), methionine (14.6%), leucine (11.2%), valine (9.5%), serine (8.5%) and tyrosine (8.1%). The change in concentration was found to be reliable only for isoleucine and phenylalanine. As compared to figures cited in the literature, isoleucine content on the 30th day of hypokinesia (0.79±0.01 mg%) either remained in the physiological range [14, 15, 17, 18], or was below it [16] and mean values [7, 12-15, 19-21]. Isoleucine concentration was below the mean (0.82±0.01 mg%) established by us in our study of 124 people under ordinary living conditions. On the 30th day of hypokinesia, phenylalanine content of plasma (0.79±0.01 mg%) remained in the range of physiological fluctuations according to [16] and was close to mean values according to [12-15, 17, 18, 20, 21] and our data listed in Table 1.

On the 30th day of hypokinesia, the concentrations of most amino acids continued to be in the range of "approximate data for adults" [18]. Only aspartic acid concentration was still below this norm. In some individuals, lysine and glutamic acid concentrations exceeded the top of the "normal" range, as they did in prior readings. During this period of our studies, methionine concentration came even closer to the bottom of the range of "approximate data" [18].

As compared to the base period status, there were higher concentrations of lysine, threonine, alanine, arginine, aspartic and glutamic acids, histidine and glycine. The concentrations of phenylalanine, cystine and proline remained at virtually the base level. At the same time, concentrations of valine, leucine, methionine, isoleucine and tyrosine were lower than under ordinary living conditions. The decrease was reliable for isoleucine concentration.

The overall indicators of levels of 17 free amino acids in plasma of our subjects, as calculated according to their status on the 30th day of hypokinesia (see Table 2), warrant the conclusion that total amino acids (E + NE) and total essential amino acids (E) were very close to the initial status. However, the sum of nonessential amino acids was somewhat higher, so that the E/NE ratio decreased. It should be noted that the demonstrated changes were unreliable.

By the 30th day of hypokinesia, as compared to the status on the 15th day, there was some increase in concentration of cystine (to almost the base status), as well as arginine, histidine, glycine and glutamic acid (see Table 3). The increase in concentrations of arginine and glutamic acid in the second 15 days of hypokinesia was more intensive than in the first 15 days. Conversely, the increase in plasma level of glycine slowed down in this period. The above-mentioned decrease in histidine concentration after the first 15 days was followed by elevation by the 30th day to a level that exceeded the status before the start of our studies. Methionine concentration diminished even more by the 30th day. It decreased by virtually the same value in the first and second 15 days of hypokinesia. Mean concentration of tyrosine continued to decrease insignificantly by the 30th day, but more intensively than by the the 15th day. As compared to the status on the 15th day, there was also a decrease in concentration of phenylalanine, which is a precursor for synthesis

of tyrosine, by the 30th day. Thus, there was a tendency toward decline of concentrations of most amino acids on the 30th day of hypokinesia, as compared to the status on the 15th day. The concentrations of seven amino acids were even lower than in the base period. They remained higher only for three amino acids. We were impressed by the fact that the concentrations of all 7 essential amino acids had a tendency toward decline by the 30th day, as compared to the status by the 15th day of hypokinesia.

With increase in duration of hypokinesia, when there was stricter adherence to identical physical activity and diet, it would seem that we could expect a decrease in differences in amino acid levels in plasma of our subjects, as compared to the individual differences in the base period. As can be seen in Table 3, parameter σ diminished for 8 amino acids on the 15th day of hypokinesia, as compared to the base period, it did not change for 3 and increased for 6 amino acids. On the 30th day, this parameter decreased for 13 amino acids, remained unchanged for 1 and increased for 3. The impression is gained that the leveling off of amino acid levels did indeed occur as duration of hypokinesia increased under identical living and diet conditions. This trend was also observed for the summary indicators (see Table 2). At the same time, the individual differences in concentrations even increased for some amino acids (alanine, threonine, cystine).

The sum of amino acids in blood plasma decreased on the 30th day, as compared to the 15th, due to decrease in sum of essential amino acids, with relatively stable sum of nonessential ones. For this reason, the E/NE ratio decreased due to decrease in plasma levels of essential amino acids.

These dynamics of amino acid levels in plasma warrant the assumption that the rise in concentration of most plasma amino acids, which occurred on the 15th day of hypokinesia, started to slow down by the 30th day and even change to decline.

On the whole, there is the impression that there was development of some decline in levels of primarily essential amino acids by the 30th day, as compared to the status on the 15th day. This could be due to several causes: in the first place, decreased passage into plasma of essential amino acids from endogenous sources due to completion of the intensive process of adaptation to hypokinetic conditions and attenuation of catabolic processes related to muscular atrophy, etc.; in the second place, systematic intake with food of smaller amounts of essential amino acids, particularly methionine, than in the base period; in the third place, possible change in absorption of amino acids taken with food from the intestine. It appears less probable that the cause is an increase in essential amino acid requirements under hypokinetic conditions, as compared to the base period, when muscular activity was definitely greater. As for the decrease and increase in plasma concentrations of some nonessential amino acids, along with the nutritional factor and possibility of supplementing their pool from endogenous sources, when analyzing the dynamics of their levels in plasma one should also take into consideration the intensity of their synthesis in the body, which is controlled by enzymatic systems in accordance with requirements under specific living conditions.

One must take into consideration a number of factors when analyzing the demonstrated dynamics of amino acid metabolism. Evidently, some change and adaptation of the body and metabolism to new living conditions had already taken place by the 30th day of hypokinesia. There was also change in proportion of anabolic and catabolic processes, as compared to the base period and 15th day of hypokinesia. Apparently, there was decrease in intensity of catabolic processes, which were more intensive during the period of acute adaptation to hypokinesia in the first 15 days. During this period, the pool of free amino acids of plasma could be built up, as usual, by intake of food, but more intensively due to more marked protein breakdown. These processes were more balanced, to some extent, by the 30th day. The low alanine content in the base period was followed by an increase in its concentration on the 15th and 30th days, probably due to decreased energy requirements of the body and adequate intake of carbohydrates. Evidently, the methionine and cystine content of the food allowance was somewhat lower during the period of hypokinesia, which led to decrease in quantity of methionine in plasma on the 15th and 30th day of hypokinesia.

Apparently, it is necessary to draw blood more often for analysis, investigation of dynamics in the recovery period and study of individual fluctuations in blood plasma amino acid levels in response to changes in the set of living and nutritional factors, in order to define the dynamics of amino acid metabolism at the early and subsequent stages of adaptation to hypokinesia.

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HUMAN STOMACH MOTOR AND EVACUATORY FUNCTIONS DURING ANTIORTHOSTATIC HYPOKINESIA

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[Article by K. V. Smirnov, A. N. Petrusenko and A. P. Menshchikov]

[English abstract from source] After overnight fasting test subjects exposed to head-down tilt showed an increase in the amplitude of stomach biopotentials, thus suggesting an increase in its contractile force. A provocative food test demonstrated an increase in the excitability of the stomach neuromuscular apparatus due to 30-day head-down tilt, which included an increment of contraction amplitudes and rates. The amplitude increase occurred both before and after food intake. However, an analysis of the wave amplitude composition showed a shift to the right which was most distinct in the fasting state. This indicated that the stomach motor activity in the digestive period showed greater resistance to head-down tilt. An increase in the asymmetry coefficient before and after food intake proportional to the head-down tilt duration suggests that the stomach evacuatory activity was inhibited.

[Text] It has now been convincingly demonstrated that there are changes in the human and animal digestive tract under the influence of weightlessness and hypokinesia [1, 2]. Most often, clinostatic hypokinesia and antiorthostatic [head-down tilt] hypokinesia (AOH) are used as the "terrestrial" model of weightlessness. In this regard, it was of special interest to make a study of electrophysiological activity of the human stomach during 30 days of -8° AOH.

Methods

This study was conducted on 9 male volunteers, in whom AOH was produced by bedrest for 30 days, with the head end of the bed tilted down at an angle of -8°. Bioelectrical activity of the stomach was examined using an EGS-4M electrogastrograph. We used the unipolar method of deriving gastric bioelectric potentials [4]. The electrogastrograms were recorded on a fasting stomach and immediately after intake of a 10% toast breakfast for 40 min, which enabled us to assess the stomach's reaction to the food load. In processing the obtained electrogastrograms, we took into consideration the frequency and amplitude

characteristics of the waves [5, 6]. We examined evacuatory function of the stomach by calculating the coefficient of asymmetry of electrogastrographic wave depolarization and repolarization time [7].

The coefficient of asymmetry was determined by the ratio of duration of depolarization phase for each peristaltic wave to duration of the phase of its repolarization. Duration of depolarization phase was determined by the horizontal projection of the ascending peak of the electrograstrographic wave, while duration of the repolarization phase was determined from the projection of the descending part of the wave. The evacuatory peristaltic waves of the pyloroantral part of the stomach coincide with electrophysiological waves with positive right-sided asymmetry ($K_a<1$), while the churning waves coincide with the electrographic waves with negative left-sided asymmetry ($K_a>1$).

Results and Discussion

Background amplitude of gastric potentials constituted 0.116±0.005 mV (Table 1). The functional test with food load elicited a 15% increase in amplitude of potentials of gastric EGG waves. By the 25th min after intake of test meal, the amplitude of gastric bioelectric potentials already exceeded its fasting value by 50%. By the 40th min, the amplitude of potentials diminished somewhat, exceeding the preprandial level by 40%. There was no appreciable change in rhythm of contractions after intake of test breakfast (Table 2). In the background period, there was prevalence of evacuatory gastric activity before the meal. After intake of test breakfast, the type of motor activity remained the same up to the 15th min. By the 25th min of the digestive period there was increase in coefficient of asymmetry (Table 3), which was indicative of change from evacuatory to churning activity. By the 40th min, evacuatory activity of the stomach increased again. During the period of hypokinesia we observed changes in amplitude of gastric bioelectric potentials. Thus, on the 4th day of hypokinesia there was some decrease of amplitude. Starting on the 8th day, the amplitude increased to 156%. On the 26th day it constituted 145% of the background level.

The functional meal test revealed substantial changes in reflex response of the stomach under hypokinetic conditions. Starting on the 4th day of hypokinesia there was greater increment in amplitude in the 5th, 15th and 25th min after intake of test meal to 120, 140 and 157%, respectively. Thus, we can refer in this instance to increased excitability of muscles of the gastric wall.

An analogous increase in gastric reflex response was recorded throughout the period of hypokinesia, with the exception of the 8th day. At this time, the absolute amplitude in the first 15 min after intake of test meal was below the fasting level, although it did exceed the background level.

On the 8th day, we observed a more profound decrease in amplitude, as compared to the background, by the 40th min, which exceeded the fasting level by only 10%. This is a 4 times greater decline than in the background period. This distinction of dynamics of amplitude of gastric contractions persisted throughout the period of hypokinesia and was the most marked on the 8th and 20th days. At these times, 40 min after the functional test with a food load, the amplitude of electrogastrographic waves decreased even below the corresponding fasting level.

Table 1. Indicator of amplitude of gastric EGG waves during 30-day AOH

Day of AOH	Phases of physiological state of stomach												
	fasting		digestive period (time after food intake), min										
			5			15			25			40		
	$M \pm m$	P_1	$M \pm m$	P_1	P_2	$M \pm m$	P_1	P_2	$M \pm m$	P_1	P_2	$M \pm m$	P_1	P_2
Background	0,116 ±0,005	—	0,131 ±0,007	—	>0,05	0,15 ±0,011	—	>0,05	0,173 ±0,015		<0,01	0,159 ±0,012	—	<0,01
4	0,113 ±0,007	>0,05	0,134 ±0,006	<0,05	>0,05	0,161 ±0,007	>0,05	<0,01	0,177 ±0,003	>0,05	<0,01	0,127 ±0,11	>0,05	>0,05
8	0,178 ±0,005	<0,01	0,168 ±0,007	<0,01	>0,05	0,168 ±0,011	>0,05	>0,05	0,148 ±0,015	>0,05	>0,05	0,132 ±0,012	>0,05	<0,01
20	0,166 ±0,008	<0,01	0,202 ±0,013	<0,01	<0,05	0,185 ±0,009	<0,01	>0,05	0,154 ±0,008	>0,05	>0,05	0,159 ±0,01	>0,05	>0,05
26	0,172 ±0,011	<0,01	0,196 ±0,013	<0,01	>0,05	0,181 ±0,009	<0,01	>0,05	0,238 ±0,014	<0,01	<0,01	0,194 ±0,11	<0,05	>0,05

Note: Here and in Tables 2 and 3, P_1 refers to reliability of differences between background and duration of hypokinesia at each phase of the study, P_2 refers to reliability of differences in phase of digesting and fasting at each stage of study.

Table 2. Effect of 30-day AOH on frequency of gastric EGG waves

Day of AOH	Phases of physiological state of stomach												
	fasting		digestive period (time after food intake) min										
			5			15			25			40		
	$M \pm m$	P_1	$M \pm m$	P_1	P_2	$M \pm m$	P_1	P_2	$M \pm m$	P_1	P_2	$M \pm m$	P_1	P_2
Background	2,7 ±0,043	—	2,76 ±0,07	—	>0,05	2,86 ±0,072	—	>0,05	2,76 ±0,083		>0,05	2,82 ±0,058	—	>0,05
4	2,82 ±0,058	>0,05	2,46 ±0,87	<0,01	<0,01	2,67 ±0,058	<0,05	>0,05	2,79 ±0,057	>0,05	>0,005	2,75 ±0,115	>0,05	>0,05
8	2,64 ±0,054	>0,05	2,70 ±0,79	>0,05	>0,05	2,77 ±0,056	>0,05	>0,05	2,66 ±0,08	>0,05	>0,05	2,88 ±0,073	>0,05	<0,02
20	2,76 ±0,069	>0,05	2,99 ±0,09	<0,05	<0,05	2,97 ±0,084	>0,05	>0,05	2,92 ±0,098	>0,05	>0,05	2,97 ±0,093	>0,05	>0,05
26	2,69 ±0,072	>0,05	2,99 ±0,078	<0,05	<0,01	2,97 ±0,085	<0,05	<0,01	2,92 ±0,094	>0,05	>0,05	2,75 ±0,070	>0,05	>0,05

Table 3. Indicator of evacuatory activity--asymmetry coefficient during 30-day AOH

Day of AOH	Phases of physiological state of stomach: fasting		digestive period (time after food intake) min: 5			15			25			40		
	$M \pm m$	P_1	$M \pm m$	P_1	P_3	$M \pm m$	P_1	P_3	$M \pm m$	P_1	P_3	$M \pm m$	P_1	P_3
Background	0,926 ±0,014	—	0,931 ±0,036	—	>0,05	0,848 ±0,023	—	<0,01	1,029 ±0,024	—	<0,01	0,932 ±0,025	—	>0,05
4	0,976 ±0,016	<0,05	0,948 ±0,033	>0,05	>0,05	0,912 ±0,029	>0,05	<0,05	0,989 ±0,03	>0,05	>0,05	0,832 ±0,043	<0,05	<0,01
8	0,912 ±0,02	>0,05	1,210 ±0,04	<0,01	<0,01	1,10 ±0,03	<0,01	<0,01	1,111 ±0,023	<0,05	<0,01	1,111 ±0,033	<0,01	<0,01
20	0,976 ±0,013	>0,05	0,976 ±0,013	<0,05	>0,05	1,032 ±0,033	<0,01	<0,01	1,061 ±0,025	>0,05	>0,05	0,982 ±0,028	>0,05	>0,05
26	1,131 ±0,019	<0,01	0,960 ±0,03	>0,05	<0,01	0,944 ±0,027	<0,05	<0,01	1,061 ±0,028	<0,05	<0,05	1,079 ±0,022	<0,01	>0,05

Thus, during hypokinesia the amplitude of gastric contractions increased with a fasting stomach and soon after intake of test breakfast (5th-25th min). At the same time, there was depletion of the capacity to maintain for a long time the intensity of electrophysiological activity of the stomach in the period of digestion.

Examination of rhythm of gastric contractions both fasting and during digestion failed to demonstrate reliable changes. The functional food test enabled us to demonstrate changes in the gastric frequency reaction. Thus, on the 4th day of hypokinesia, there was a reliable decrease to 90% in frequency of gastric contractions within the first 5 min after intake of food. Starting on the 8th day, there was gradual restoration of frequency response to intake of test meal. There was increase in contraction frequency increment with increase in duration of hypokinesia: while it constituted 2% in the first 5 min after intake of test meal in the background period, this parameter constituted 8% on the 20th experimental day and reached its highest value, 11%, on the 26th day.

The changes in composition of variation series of amplitude distributions are also interesting. On a fasting stomach, in the background period, the first 3 classes of amplitudes (0.05-0.15 mV) constituted 80% of the total (35-30-15% for the 1st, 2d and 3d classes, respectively). In the wave range of 0.15 to 0.3 mV (4th, 5th and 6th classes) there were 19% of all waves in the sample (9.9-5.3-3.8%). Only 3% of the waves were referable to the range of 0.4 to 0.45 mV. We observed no waves with higher amplitude when fasting in the background period.

A qualitative change in distribution of wave amplitudes was demonstrated starting on the 4th day of hypokinesia. There was a gradual percentile decline

in the low-amplitude range (0.05-0.15 mV) from 75 in the background period to 57% on the 26th day of hypokinesia, with concurrent increase in number of waves in the next, higher classes (0.15-3.0 mV) from 20% in the background period to 30% on the 26th day of hypokinesia, which was indicative of increased contractile activity of the stomach. We observed appearance of an additional group of waves, even higher in amplitude, which had not been seen in the base period. They were distributed in the classes of 0.5 to 0.9 mV. While there were 3% waves in the range of 0.35 to 0.45 mV in the background period, this range was referable to 7, 8, 12 and 15% of the waves on the 4th, 8th, 20th and 26th days, respectively.

Some change in the variation series of amplitudes was also noted in the period of digestion, with a general tendency toward a shift to the right. On the 20th day of hypokinesia there was an 8% decrease in low-amplitude (0.05-0.15 mV) waves and 7% increase in waves referable to the medium range (0.15-0.30 mV).

The most marked shift of amplitude composition of waves to the right was observed in fasting subjects, which is apparently indicative of greater resistance of gastric activity to AOH in the digestive period.

According to the coefficient of asymmetry, evacuatory activity of the stomach also underwent changes during hypokinesia, with gradual change from evacuatory nature in the fasting background to churning. Prevalence of churning type of waves over evacuatory type leads to stasis of gastric contents. Evacuatory activity in the period of digestion also changed under the influence of hypokinesia.

On the 4th day, there was increase in intensity of evacuatory processes in the stomach with decline in values of coefficient of asymmetry, as compared to the background level. From the 8th day on, there was already persistent prevalence of mixing activity over evacuatory, which persisted in the digestive period for the duration of hypokinesia.

The conclusion that evacuatory activity of the stomach slows down, which we derived on the basis of increase in coefficient of asymmetry, is consistent with findings [8] in a study that established the fact of slower evacuation of food from the canine stomach using a roentgenological method.

The increased increment of amplitude and frequency of electrogastrograms in the first 5 min after intake of the test breakfast is indicative of a more marked reflex reaction by the stomach's neuromuscular system.

The observed increase in amplitude of electrogastrographic waves is indicative of greater force of contractions, which is typical of the phenomenon of the so-called irritated stomach.

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CIRCADIAN PATTERN OF SIMIAN FUNCTIONAL PARAMETERS DURING HYPOKINESIA AND IN THE RECOVERY PERIOD

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 3, May-Jun 84 (manuscript received 1 Mar 83) pp 38-43

[Article by N. F. Kolpakova and T. G. Urmancheyeva]

[English abstract from source] Seven male rhesus monkeys, aged 3.5-4 years, were examined during clinostatic hypokinesia for 20-40 days and after exposure for 16 days. Parameters of the cardiovascular function, external respiration and body temperature were measured. During and after hypokinesia the amplitude of diurnal variations of heart rate tended to decrease. The position of heart rate acrophases shifted most during the first 3 weeks of hypokinesia and during recovery. Changes in the amplitude of diurnal variations of arterial pressure were different. The position of acrophases on the time axis was unstable and tended to recover by hypokinesia days 30-40 and then shifted again on the 1st recovery day. The amplitude of diurnal variations of the respiration rate increased, the position of acrophases on the time axis shifted and their width changed. By the 14th day of readaptation the diurnal dynamics of this parameter tended to recover. During hypokinesia the amplitude of diurnal variations of body temperature increased or decreased and the position of acrophases on the time axis remained stable.

[Text] As shown in the studies of several authors [1, 2], primates are characterized by distinct, mainly monophasic circadian periodicity of physiological functions. At the same time it was established that exposure to factors that lead to development of chronic emotional stress and neurosis disrupts the circadian rhythms of these animals. It is also known that, under hypokinetic conditions, both man and animals develop signs of negative psychoemotional stress [3], along with specific changes.

In view of the foregoing, it is deemed important to determine the distinctions of the circadian dynamics of vital functions of monkeys under hypokinetic conditions when investigating the effects of prolonged restriction of motor activity.

Our objective here was to investigate the diurnal dynamics of some parameters of the cardiovascular system and external respiration, as well as body temperature at different stages of clinostatic hypokinesia and recovery of monkeys.

Methods

This work was done with 7 Macaca rhesus male monkeys 3.5-4 years of age, weighing 4.5-5 kg. Before the experiment, all of the animals were adapted to staying in primatological chairs (for 2-3 months). We performed 3-5 background experiments on each monkey, in the course of which we regularly recorded pulse rate (PR), respiration rate (RR), rectal temperature (RT) and blood pressure (BP) taken by the indirect Korotkov method at specific times of day (1200, 1600, 2000, 2400, 0400 and 0800 hours).

A previously described method [4] was used to restrict movement during clinostatic hypokinesia. Hypokinesia lasted 20 to 40 days, and the monkeys were studied for 15 days of the recovery period. The above parameters were recorded on the 2d, 10th, 20th, 30th and 40th days of hypokinesia, 2d, 7th and 15th days of the recovery period.

The circadian rhythm of the studied clinicophysiological parameters of the monkeys was evaluated individually at all stages of the experiment (base data, hypokinesia, recovery). The nonparametric analytical method [5] was used to determine the timing of acrophases (minimum and maximum of the tested clinicophysiological parameters at different stages of the experiment).

Results and Discussion

The circadian dynamics of PR, RT, RR and BP conformed to the norm in all of the experimental monkeys in the initial experiments.

As was previously reported, with prolonged exposure to clinostatic hypokinesia the monkeys showed decline of body temperature, negative fluid balance, weight loss and decrease in volume of lower extremities. There were changes in different directions in parameters of the cardiovascular, respiratory and hemopoietic systems, and functional state of the brain, mainly on the cortical level [6-8].

Changes developed in diurnal pattern of the parameters studied starting on the 1st day of limited motor activity in monkeys that were in horizontal position. We observed both high individual variability of changes and diversity of configurations of 24-h curves for the same parameter in the same animal at different periods of clinostatic hypokinesia.

Data obtained on all animals before hypokinesia, at the indicated days of hypokinesia and recovery period were combined on the time axis in order to demonstrate the general trend of changes in position of acrophases (minimum and maximum values of parameters recorded over the 24-h period).

Circadian rhythm of PR was the least stable in hypokinetic monkeys.

In the base experiments (Figure 1), the amplitude of daily fluctuations (ADF) of PR was in the range of 14 to 35/min in monkeys Nos 3, 4, 5, 7, and from 47 to 56/min in monkeys Nos 1 and 2. During hypokinesia and the recovery period, considerable impairment of circadian rhythm was observed in most cases with regard to PR, manifested by decrease in amplitude of daily fluctuations of this parameter. For example, in monkey No 1, PR ADF decreased during the periods of hypokinesia and recovery, in comparison to the base value. The most significant smoothing of daily curves for this parameter was present in the recovery period; on the 7th day of readaptation ADF of pulse rate decreased by 93%. On the 15th day of the recovery period, 2 animals (Nos 2 and 7) presented a tendency toward normalization of ADF of pulse rate.

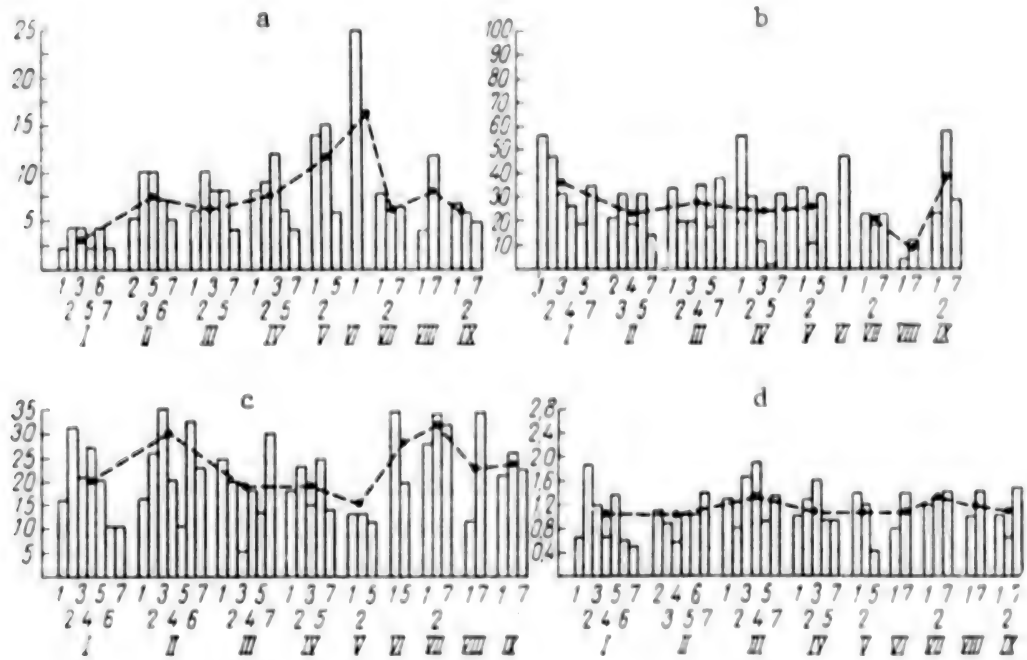

Figure 1. Amplitude of daily fluctuations of respiration rate (a), pulse (b), blood pressure (c) and body temperature (d) in background experiments (I), during hypokinesia (2, 10, 20, 30 and 40 days, II-VI, respectively) and recovery period (2d, 7th and 15th days, VII-IX, respectively)

X-axis, stages of experiment. 1-7) monkey numbers. The dash line shows mean ADF values.

In the base experiments, the acrophase of pulse minimum was referable to the time from 2000 to 0800 hours and maximum, 1200-1600 hours (Figure 2). Under hypokinetic conditions, there was a shift in acrophase position on the time scale. More significant changes in timing of pulse acrophases occurred on the 2d, 10th and 20th days of hypokinesia; the shift in acrophase position was also substantial in the recovery period. ADF of mean dynamic pressure (MDP) was in the range of 10-31 mm Hg in the initial experiments (see Figure 1). ADF of MDP increased throughout the period of hypokinesia and recovery in 3 monkeys (Nos 1, 6, 7); the only exception was the 7th day of the recovery period for

monkey No 1, in which this parameter declined. The most significant increase in ADF of MDP was observed in animal No 7 on the 2d and 10th days of hypokinesia and on the 2d, 7th and 15th days of the recovery period, when amplitude increased by 2.5-3.5 times. In another group of animals (Nos 2, 3, 4 and 5), ADF of MDP decreased during hypokinesia and in the readaptation period, as compared to initial values. At the same time, on the 2d day of the recovery period ADF of MDP increased by 13%, as compared to base value, in monkey No 2, by 72% in monkey No 3 on the 2d day of hypokinesia and by 26% on the 20th day of hypokinesia in monkey No 5.

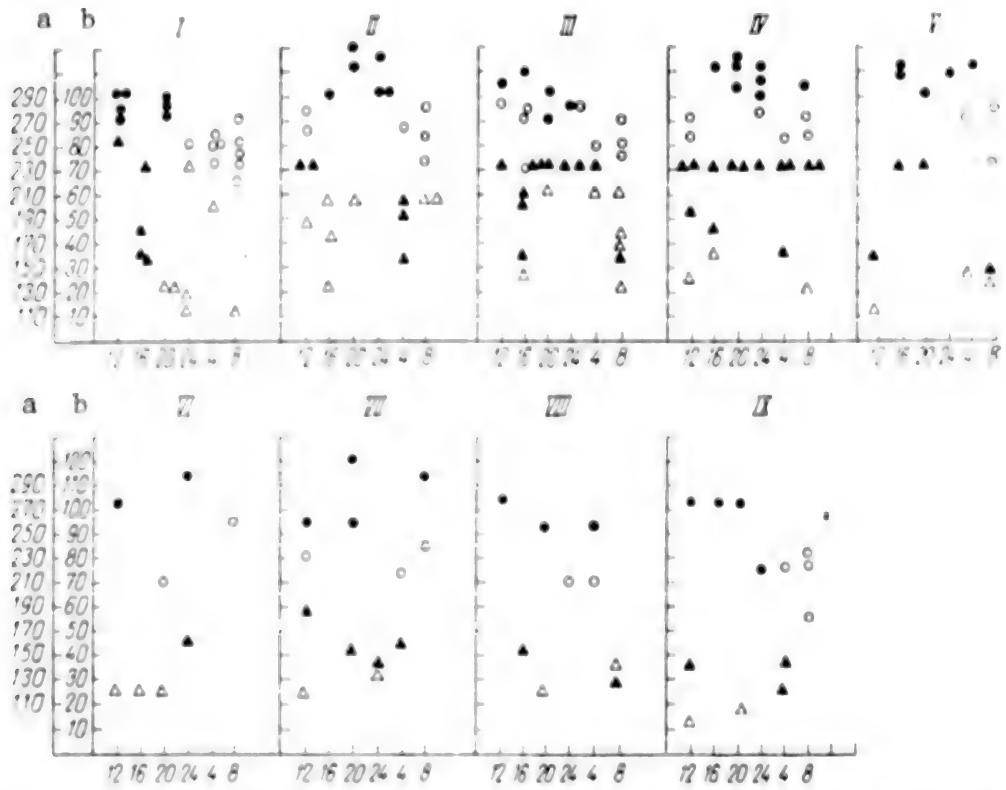

Figure 2. Position of acrophases of PR (a, per min) and BP (b, mm Hg) on time axis in background experiments (I) and at different stages of clinostatic hypokinesia (II-VI, corresponding to 2d, 10th, 20th, 30th and 40th days) and recovery (VII-IX, corresponding to 2d, 7th and 15th days.

X-axis, time of day (hours). Dark and white circles are acrophases of BP maximum and minimum, respectively; dark and white triangles, the same for pulse rate.

In the base experiments (see Figure 2), the acrophase of maximum mean dynamic blood pressure was in the range of 1200-2000 hours and minimum, 2400-0800 hours. On the 2d day of hypokinesia, the minimum acrophase was referable to two time periods, 1200 hours and 0400-0800 hours; maximum acrophase shifted by 3 h, to 1600-2400 hours. On subsequent days of hypokinesia (10th-20th days) the acrophase of the maximum remained more stable, being referable to 1200-2400 hours.

The minimum acrophase on the 10th day of hypokinesia coincided with two time periods, 1200-1600 and 0400-0800 hours. On the 20th day of hypokinesia, there was a change in position of minimum acrophase in the first time period; it became shorter than on the 10th day by 3 h (1600 hours), while the second period remained unchanged, 0400-0800 hours. There was a less marked shift of acrophases on the 30th-40th days of hypokinesia. The acrophase shift increased again on the 2d day of the recovery period, and relative normalization was observed on the 15th day.

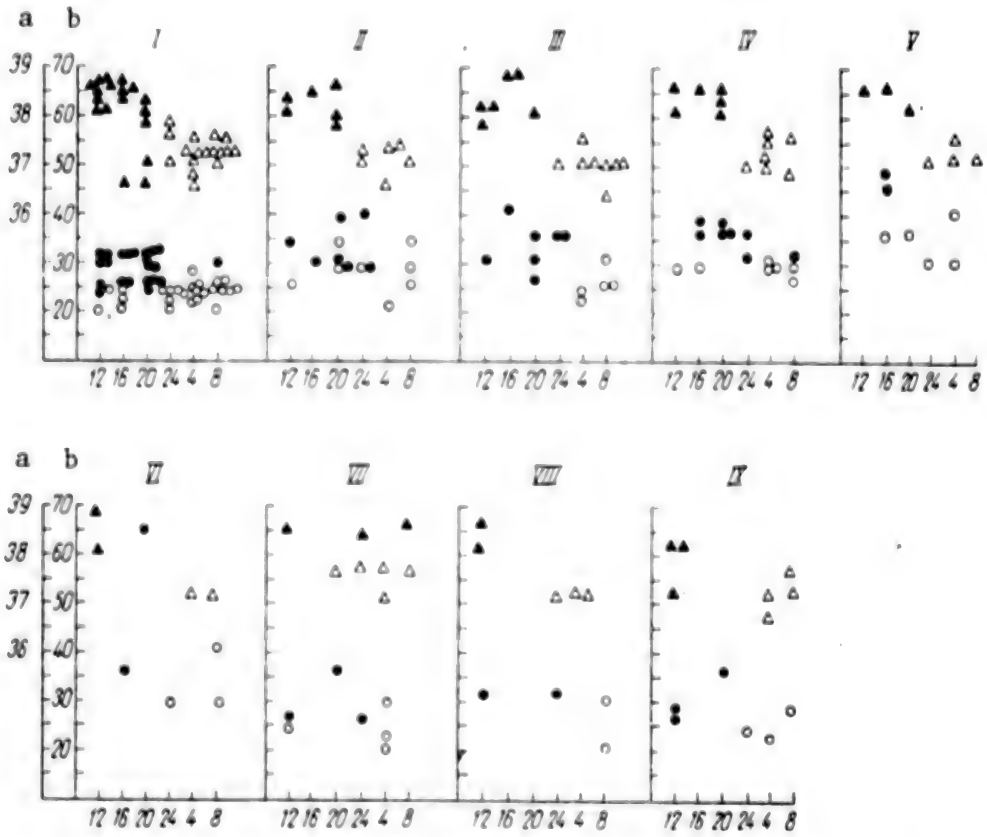

Figure 3. Position of acrophases for TT (a, °C) and RR (b, per min) on time axis in background experiments (I), at different stages of clinostatic hypokinesia (II-VI corresponding to 2d, 10th, 20th, 30th and 40th days) and recovery period (VII-IX, corresponding to 2d, 7th and 15th days).

X-axis, time of day (hours). Dark and white circles--acrophases of maximum and minimum RR, respectively; dark and white triangles, same for TT [body temperature].

Figure 1 illustrates the dynamics of ADF for RR in all experimental animals. In the base experiments, this parameter was in the range of 2-4/min. With limited motor activity, all animals showed an increase in amplitude, which persisted at all subsequent stages of hypokinesia and recovery. At the same time, we should mention some individual differences in dynamics of ADF of RR of monkeys under experimental conditions. In some of them, for example,

monkey No 1, the amplitude increased with increase in duration of hypokinesia, whereas in others the increase was followed by a decrease. During the recovery period there were also changes, in different directions, in ADF of RR: this parameter diminished in relation to amplitude under hypokinetic conditions in some animals (Nos 1 and 2), while still above the base value) and increased in others, in relation to both the base value and hypokinetic period.

The acrophase of RR maximum was in the range of 1200-2000 hours and that of the minimum, 2400-0800 hours (Figure 3). The maximum acrophase on the 2d day of hypokinesia shifted to 1600-2400 hours, i.e., to the right by 3 h, while minimal RR was noted at all times of day. On the 10th day of hypokinesia, the period of maximum RR acrophase increased by 3 h (1200-2400 hours) and the minimum became shorter (0400-0800 hours). The 30th-40th days of hypokinesia were characterized by some normalization of acrophases on the time scale. On the 2d day of the recovery period, we again observed a significant shift of acrophases, which recovered by the end of the 2d week.

In the base experiments, experimental monkeys showed an ADF of body temperature (TT) in the range of 0.7-1.6°C (see Figure 1). On the 2d day of hypokinesia, 2 animals (Nos 7 and 6) showed a 100% increase in ADF of TT, while the rest demonstrated a decrease. At subsequent stages of hypokinesia and recovery, smoothing of diurnal curves was observed in monkeys Nos 2 and 5; in some cases ADF of TT decreased by 60-70% (30th day of hypokinesia, monkey No 5; 10th day of hypokinesia, monkey No 2). Regardless of the direction of changes in ADF of TT, we should mention that there was a common trend toward normalization by the 30th-40th day of hypokinesia. ADF of TT increased significantly in comparison to the base value in the recovery period in 2 animals (Nos 1 and 7) and decreased in monkey No 2.

The position of TT acrophases during hypokinesia was more stable than other parameters (see Figure 3). In the base experiments, the acrophase of TT maximum was in the range of 1200-2000 hours and TT minimum at 2400-0800 hours. These positions of acrophases persisted throughout the period of hypokinesia. But in the recovery period there was a change in position of acrophases on the time scale. On the 2d day of the recovery period, the maximum (1200, 2400, 0800 hours) and minimum (2000-0800 hours) acrophases increased. Maximum TT on the 7th day of the recovery period was concentrated at 1200 hours, the position of the minimum acrophase corresponded to its initial position (2400-0800 hours). The position of the maximum was the same at the end of the 2d week as on the 7th day of the recovery period (1200 hours), and minimum TT values were found at 2000 hours and from 0400 to 0800 hours.

Thus, the results of this study revealed that clinostatic hypokinesia is a factor that disrupts appreciably the dynamic stereotype of vital functions of monkeys, as manifested by changes in different directions in circadian pattern of functions.

N. Ye. Panferova [10], who made a study of humans, observed impairment of circadian rhythm of PR, RR, BP and TT when motor activity was restricted. She believes that impairment of the circadian rhythm of body functions is related primarily to restricted muscular activity, the general biological

significance of which consists of maintaining a specific body tone. At the same time, S. I. Stepanova [11] interprets the ADF changes in different directions, which are referable to functional activity of body systems, as an expression of stress. Changes in circadian rhythm of functions in primates have been described both during a period of neurotigenic stimuli [12] and at different times after them [9]. It has also been shown that the PR is a highly informative indicator of the emotional tension of monkeys and that the smooth circadian fluctuations of pulse rate are inherent in monkeys with experimental neurosis [13].

The change in position and width of zones of acrophases of the tested functional parameters on the time axis is indicative of significant strain on adaptation mechanisms [14]. The changes demonstrated in this study in circadian rhythm of primate functions during long-term clinostatic hypokinesia are consistent with the conception that desynchronosis is a mandatory element of the general adaptation syndrome [14, 15]. The latter, including emotional stress in experiments with monkeys, is apparently one of the prime factors determining the body's reaction, along with the specific effects of hypokinesia in horizontal position (hydrostatic factor, hypodynamia, changes in proprioception, etc.).

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DYNAMICS OF RED BLOOD CELL CHANGES IN RATS DURING ACUTE IMMOBILIZATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 3, May-Jun 84 (manuscript received 10 Mar 83) pp 43-47

[Article by L. N. Katyukhin and M. N. Maslova]

[English abstract from source] The standard clinical parameters of red blood, morphometric characteristics, membrane resistance and electrolyte balance of red blood cells of white rats exposed to acute immobilization were investigated. It was found that the immobilization of rats in small-size cages produced statistically significant changes in the concentration of ascorbic acid in the adrenals and oxycorticosteroids in plasma, as well as erythrocytosis, reduction of red blood cell size, planocytosis and decrease of intracellular sodium. The above parameters did not return to the norm 24 hours after 3-hour immobilization. It is suggested to use the amount of plasma per red blood cell as a stress-marker in red blood.

[Text] The general adaptation syndrome [1] develops when there is substantial change in the environment. Hypokinesia, as a factor that depresses the "freedom" instinct, is considered to be one of the strongest stressors. In the work of H. Selye and his school, as well as studies of Soviet authors, nonspecific white blood cell changes were demonstrated that are inherent in the "anxiety" stage [2-5]. There are some works dealing with the effect of acute immobilization of animals on erythrocytes [6-9]. Because of the simplicity of obtaining and accessibility to investigation, it is deemed justified to search for reliable criteria to assess stress states on the basis of red blood cell indications. Nevertheless, the question of early period of development of the hypokinetic syndrome in the red blood system has still not been sufficiently elucidated.

We examined here the parameters of rat blood, which are used in clinical practice, at different stages of acute immobilization and in the recovery period, as well as morphometric parameters, membrane resistance and electrolyte balance of erythrocytes and plasma.

Methods

The studies were conducted on 49 white Wistar rats weighing 180-200 g, in the morning on a fasting stomach. To restrict the animals' activity, they were

placed in tight individual cages made of plexiglas, belly down. The rats were decapitated 10 and 180 min after immobilization, 1, 3 and 24 h after termination of 180-min immobilization. Control animals were sacrificed at the same times. We assayed in heparinized blood erythrocytes, total hemoglobin, hematocrit and pH. The Price-Jones curves were determined from smears stained according to May-Grunwald, Romanovsky and Giemsa. We measured mean volume, thickness, area, spherical index and specific surface of erythrocytes [10]. Determination was made of osmotic [11], acid [12] and mechanical [13] resistance of red cell membranes. Concentrations of potassium, sodium, calcium and magnesium in erythrocytes and plasma were assayed by flame photometry and atom-absorption spectrometry. The stressor reaction was evaluated on the basis of decrease in weight of the spleen and concentration of ascorbic acid in the adrenals [14]. In several experiments, we assayed 11-hydroxycorticosteroids (11-HCS) in blood plasma [15].

Results and Discussion

The experiments established that a statistically significant reduction in spleen weight and concentration of ascorbic acid in the adrenals (Figure 1) occur within the first minutes of immobilizing the animals. After immobilization for 180 min, 11-HCS of plasma increased by 92% and constituted $0.242 \pm 0.026 \cdot 10^{-3}$ g/ℓ. A trend toward restoration of this parameters is evident immediately after the rats are released from the cages, and 1 day later the differences from control animals were unreliable. The change in acid-base state was caused only by immobilization: after 10 min pH decreased by 0.13 (Table 1). Immobilization for 3 h did not cause acidosis. A higher red cell count was noted in peripheral blood from the first minutes to the end of the observation period. There was a corresponding increase in hematocrit and hemoglobin concentration; however, already 1 h after 180-min immobilization these parameters did not differ from base values. Erythrocyte hemoglobin concentration was low, and this was closely related to decrease in cell volume. Nevertheless, there were no changes in their distribution according to diameter under stress and in the first hours of recovery. It is only 1 day later that the Price-Jones curve shifted to the left and mean diameter decreased. For this reason, we calculated the geometric parameters of a red cell in control and experimental animals (Table 2). We found that the erythrocyte profile changed under stress: a high number of wandering cells, as indicated by the diminished thickness and increased spherical coefficient, was inherent in the period of acute immobilization and early hours of recovery. In addition, the

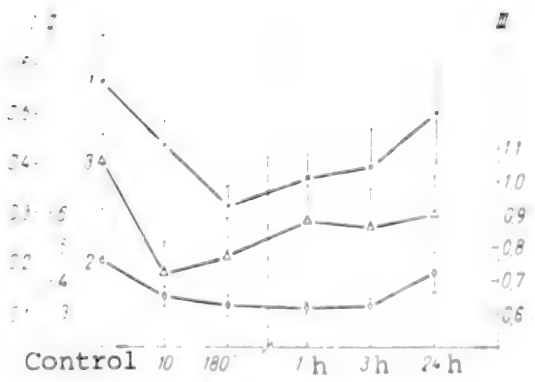

Figure 1.
Dynamics of changes in weight of spleen (1), concentration of ascorbic acid in adrenals (2) and K indicators (3) in control and experimental rats after immobilization and in recovery period

Y-axis: I) spleen weight (g)
II) ascorbic acid concentration
III) K ($\cdot 10^{-13}$ ℓ)

the red cell acquired some reserve surface area: there was reliable increase in specific cell surface. With hemodynamics under stress, the reduced dimensions of red cells, along with increase in deformation properties, facilitate their passage through narrow capillaries. After 24 h, the shape of circulating erythrocytes is restored, but their dimensions are still reduced, with statistical significance, as compared to erythrocytes of control animals.

Table 1. Blood parameters of control and experimental rats after immobilization and during recovery period (n = 7)

Examination time	Hematocrit, relative units	Erythrocyte count, $\times 10^{12}$ I/ℓ	Hemoglobin, g/ℓ	Mean hemoglobin per erythrocyte, pg	Mean Hb concentration per erythr, g/ℓ	pH, relat. units
Control	0,383±0,008	5,85±0,24	131±3	22,5±0,6	342±3	7,39±0,01
Stress:						
10 min	0,439±0,010**	7,54±0,23**	156±6**	20,7±0,6*	354±8	7,26±0,04**
180 min	0,433±0,017**	7,47±0,40**	150±7**	20,2±0,4**	347±5	7,36±0,02
Recovery						
1 h	0,399±0,016	6,91±0,34*	133±7	19,2±0,8**	332±5	7,39±0,01
3 "	0,400±0,013	7,08±0,35**	136±6	19,2±0,4**	341±5	7,38±0,01
24 "	0,386±0,008	6,91±0,32*	131±3	18,9±0,3**	339±4	7,42±0,02
Control	0,382±0,008	5,99±0,34*	132±3	21,9±0,4**	344±3	7,39±0,1

Note: Here and in Tables 2 and 3: *P<0.05, **P<0.01, as compared to results before immobilization.

Table 2. Morphometric characteristics of red cells of control and experimental rats after immobilization and during recovery period (n = 7)

Examination time	Mean volume, fℓ	Mean diameter, μm	Mean thickness, μm	Mean surface, μm^2	Specific surface, $\mu m^2/f\ell$	Spherical index, relative units
Control	65,8±2,0	7,09±0,11	1,67±0,05	151±5	2,30±0,07	4,3±0,2
Stress:						
10 min	58,3±1,0**	7,06±0,06	1,48±0,04*	150±3	2,57±0,08*	4,8±0,2*
180 min	58,2±1,6**	7,09±0,07	1,48±0,06*	151±3	2,60±0,09**	4,8±0,2*
Recovery:						
1 h	58,0±2,0*	6,99±0,08	1,51±0,05*	147±3	2,54±0,08*	4,7±0,2*
3 "	56,8±1,6**	7,06±0,08	1,45±0,04**	150±3	2,64±0,07**	4,9±0,2*
24 "	56,2±2,1*	6,74±0,09*	1,58±0,07	136±4*	2,44±0,11	4,3±0,2
Control	64,5±3,1	7,02±0,10	1,67±0,07	148±5	2,31±0,11	4,2±0,2

There was change in strength of red cell membranes, along with change in erythrocyte profile. Thus, immediately after immobilization, a fraction of cells appeared in peripheral blood, which were highly resistant to acid hemolytic (Figure 2a). After 180 min, there was a reliable shift and elevation of the right arm on the erythrogram (Figure 2b). Evidently, the increase in acid-resistance was attributable to appearance of higher number of reticulocytes in

Table 3. Concentration of electrolytes (mmol/ℓ) in erythrocytes and plasma of control and experimental rats after immobilization and during recovery (n = 7)

Examin. time	Erythrocyte				Plasma			
	K	Na	Ca	Mg	K	Na	Ca	Mg
Control	95±1	3,8±0,1	0,07±0,01	1,97±0,09	6,6±0,2	137±1	2,41±0,04	0,68±0,02
Stress:								
10 min	95±1	2,7±0,2**	0,10±0,03	1,94±0,07	6,6±0,1	141±1*	2,54±0,02*	0,89±0,03**
180 min	94±1	3,5±0,1*	0,07±0,01	2,01±0,10	7,6±0,3**	136±1	2,29±0,03*	0,96±0,04**
Recovery:								
1 h	96±1	3,8±0,1	0,08±0,01	1,84±0,09	7,0±0,4	135±1	2,20±0,04**	0,75±0,02*
3 "	95±2	3,1±0,2**	0,07±0,01	1,94±0,10	7,1±0,6	133±1**	2,31±0,06	0,77±0,03*
23 " [sic]	94±1	4,2±0,3	0,09±0,01	1,99±0,06	6,6±0,3	136±1	2,24±0,06*	0,72±0,06
Control	94±1	3,8±0,1	0,07±0,01	2,02±0,08	6,8±0,3	138±1	2,41±0,04	0,69±0,02

blood [16, 17]. P. Resnitzky et al. [18] relate the increase in membrane resistance to hydrochloric acid to the red cell "enveloping" effect under stress due to increased plasma catecholamine levels. Thereafter, along with increase in resistant red cells, less resistant forms appear (Figure 2c and 2d). One day after stress, acid-resistance of experimental animals' erythrocytes was already reliably lower than in the control (Figure 2e).

Erythrocyte resistance to mechanical trauma diminishes right after the animals are immobilized and remains low to the end of the observation period: percentage of hemolysis constituted 9.7±0.6 in the control, 10.0±1.4 ($P<0.05$) after 10-min immobilization, 16.4±1.7 ($P<0.01$) after 180-min immobilization, 15.9±2.5 ($P<0.05$), 13.8±1.5 ($P<0.05$) and 13.6±1.2 ($P<0.05$) after 1, 3 and 24 h into the recovery period, respectively. The dynamics of red cell hemolysis in solutions with hypoosmotic concentrations of sodium chloride remained unchanged.

Table 3 lists data on levels of the most important blood cations in erythrocytes. It shows that a deviation in electrolyte balance was demonstrable from the very first minutes of immobilization. Thus, the most appreciable decline of sodium concentration in erythrocytes was noted immediately after immobilizing the animals; 3 h after 180-min immobilization of rats in the cages, there was a second decline in concentration of this cation. No deviations were demonstrable in concentrations of other electrolytes within blood cells. The changes in cation concentrations were more marked. Hyperpotassemia, for example, developed by the 3d h of immobilization and persisted for 3 h after the rats were released from cages. High magnesium levels appeared within the first min of immobilization and persisted over the 24-h observation period. There

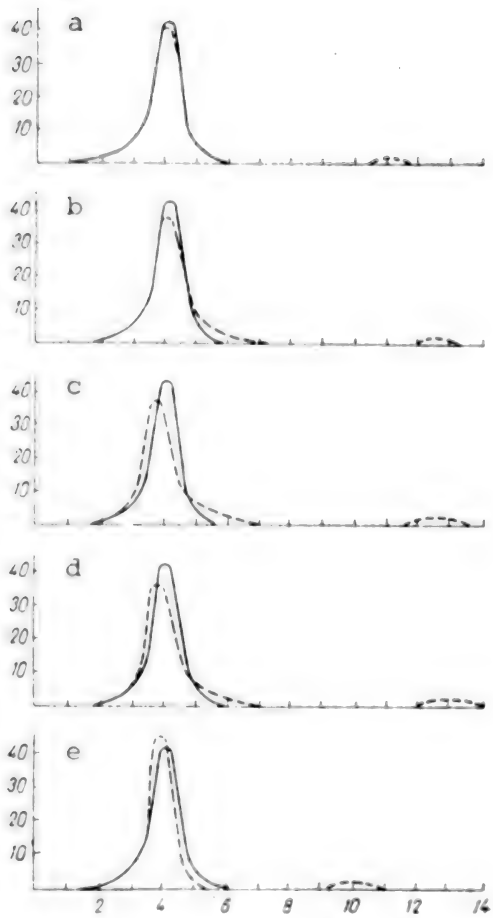

Figure 2.
Erythrograms of control (solid lines) and experimental (dash line) rats during 10- (a) and 180-min (b) immobilization and 1 (c), 3 (d) and 24 h (4) later
X-axis, time (min); y-axis, per
Y-axis, % hemolysis

were fluctuating changes in concentrations of blood plasma sodium and calcium: after increase when the rats were immobilized, there was a tendency toward decrease to the end of the experiment. Evidently, shifting of the liquid phase into the perivascular space against the background of drastic blood pressure elevation made a substantial contribution to the increase in concentrations of the tested electrolytes in blood plasma in the presence of acute immobilization stress.

As can be seen from the foregoing, the reported changes in the most accessible parameters of blood did not exceed the range of individual fluctuations, and they were adaptive rather than pathological. For this reason, in the absence of a control and without sufficient number of animals, it may be difficult to determine the status of experimental animals on the basis of red cell findings. In addition, the dynamics of development of a stress reaction and recovery of the tested parameters were extremely uneven: some recovered, others had only a tendency to do so, while others yet were not restored 1 day after immobilization and were phasic. We tried to find criteria, the absolute values of which could be used to assess the severity of physiological changes when working with animals. In our experiments, we determined the amount of plasma per erythrocyte:

$$K = 10 \frac{1 - EPV}{RBC}$$

where EPV is hematocrit (relative units) and RBC is number of erythrocytes per microliter ($\times 10^6$).

As can be seen in Figure 1, III, this criterion, which we arbitrarily named K, was close to 1 in control animals. During immobilization it diminished with a high degree of reliability and did not reach the initial value in the recovery period.

Thus, the results we obtained here indicate that, under the influence of acute immobilization, rats develop statistically significant changes in both the adopted stress markers and less widely used parameters. According to many of the measured parameters, there was virtually complete normalization 24 h after

180-min immobilization. Nevertheless, several parameters, such as mechanical and acid resistance of membranes, volume and diameter of red cells did not revert to control values for another 24 h after immobilization. The proposed criterion K clearly reflects the dynamics of functional changes in the red cell system in the presence of immobilization stress in rats, and it can be a sensitive and reliable marker of stress.

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ULTRASOUND DISTRIBUTION AND BONE CALCIUM CONTENT IN EXPERIMENTAL ANIMALS SUBMITTED TO HYPOKINESIA AND WEIGHTLESSNESS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 3, May-Jun 84 (manuscript received 1 Feb 83) pp 48-52

[Article by Yu. Zh. Saulgozis, V. Ye. Novikov, M. A. Dobelis, Ye. A. Il'in and V. I. Lebedev]

[English abstract from source] The velocity of ultrasonic propagation, calcium content and femur size of rats exposed to actual and simulated weightlessness were investigated. The exposure slowed down the ultrasonic velocity in bones. The effect of the calcium content on the ultrasonic velocity in various bone sites was different: as a rule there was a positive correlation in diaphyses and negative correlation in epiphyses. These specific features should be taken into consideration when new methods of bone ultrasonic diagnostics will be developed.

[Text] It is known that man develops significant changes in fluid-electrolyte metabolism, with increased elimination of calcium and diminished mineralization of bones, as well as other changes causing decline of mechanical characteristics of bone tissue, in the course of long-term spaceflights [1-3].

This has been confirmed in animal experiments. It was demonstrated, in particular, that there is slowing of periosteal osteogenesis and appositional bone growth [4, 5], signs of osteoporosis [6, 7], diminished mechanical strength of long bones [8, 9] and vertebrae [10] are observed under the effect of even brief spaceflights (biosatellites of the Cosmos series).

However, for a number of reasons, the results of animal studies cannot be extrapolated to man. This makes it imperative to search for noninvasive methods of monitoring the condition of bone tissue as related to the objectives of space biology and medicine.

One of the promising means of monitoring changes in mechanical properties, structure, biochemical composition of bone tissue and evaluating bearing capacity of the human skeletomuscular system is to examine tissues with ultrasound. This method is finding broad applications in clinical practice. However, there are no data about the effect of weightlessness, hypokinesia and accelerations on the rate of propagation of ultrasound in human bones.

We describe here a combined study of the effect of limited motor activity, as well as real and simulated weightlessness, on rate of propagation of ultrasound and calcium content of rat bones.

Methods

We examined the bones of Wistar rats differing in age. The animals were divided into 5 groups: the 1st consisted of rats in the vivarium control, the 2d--synchronous experiment, in which the animals were kept in a mockup of the Cosmos-1129 satellite with simulation of all spaceflight factors except weightlessness. The 3d group consisted of animals flown aboard Cosmos-1129 biosatellite and the 4th, of animals suspended on a special stand [11] in such a manner that their hind legs had no support and did not bear a functional load. The 5th group consisted of animals submitted to hypokinesia in tight box-cages. We examined the femoral diaphyses containing only compact bone of rats in the 2d and 3d groups, and in the corresponding control animals of the 1st group. These groups of animals were decapitated after 19.5 experimental days and 29-day recovery period. The 4th and 5th groups of animals and their controls in the 1st group were sacrificed after the 22d day of the experiment. The age of animals in the 2d and 3d groups was 3 months, 4th and 5th groups 2.5 and 6.5 months, and the 1st group was represented by animals 2.5, 3 and 6.5 months of age. The bones taken for the studies were cleared of periosteum and soft tissue, stored in gauze moisted with saline at a temperature of 4°C. Before the study, bone temperature was brought up to room level (20°C). The bones were moistened with saline during the experiment to prevent drying.

An ISS-1 instrument was used to examine the rate of propagation of ultrasound (c) in bones by the method of penetrating and lateral transmission at a wave frequency of 150 kHz. We determined the time of ultrasound transmission by means of a D-81 standard sensor (penetrating transmission) and a specially developed sensor with concentrators (lateral transmission). Sound was passed through each bone 4 times, alternately in proximal-distal and distal-proximal directions. This diminished the margin of error contributed by the sensor's contact with bone. We calculated the mean velocity of ultrasound in each bone from the results of 4 measurements. We covered the site of contact between the emitter and receiver with glycerin to assure good acoustical contact.

Morphometric data (width of diaphysis, thickness of cortical layer and width of bone-marrow canal) on cross sections of the diaphysis at its mid-level. The measurements were taken using a microscope equipped with ocular micrometer at a magnification of 40×. Calcium content in different parts of the femur was determined by the method of atom-absorption spectrophotometry [12]. The bones were first dried to a stable weight.

The data were submitted to mathematical processing by means of two-factor variance analysis [13]. We determined the influence of experimental conditions (factor A) and type of bone (factor B) on ultrasound velocity in bone. Factor A was represented in 3 variants: A_1--control (1st group); A_2--suspension (4th group); A_3--hypokinesia (5th group). There were also 3 variants of factor B: B_1--femur, B_2--tibia and B_3--humerus. We excluded from the uniform statistical set results, deviations of which from mean values exceeded the normalized value. Reliability of differences between the two arithmetic means for different groups was assessed by Student's criterion.

Determination of link between ultrasound velocity, on the one hand, and concentration of calcium in tissue and thickness of diaphyseal wall of the bone, on the other hand, was made by multidimensional linear correlation and regression analysis. In this study we considered the velocity of ultrasound as function Y, which depends on 4 different arguments: X_i--concentration of calcium in proximal (Ca_1, argument X_1), diaphyseal (Ca_2, X_2) and distal (Ca_3, X_3) parts of the bone and total thickness of two opposite walls of bone diaphysis (2b, argument X_4). Function Y-X_i was approximated as follows:

$$Y = B_0 + \sum_{i=1}^{k} B_i X_i,$$

where $k = 4$ is the number of arguments considered. Coefficients B_0, B_1, B_2, B_3 and B_4 were determined by the least squares method from experimental data.

Results and Discussion

According to the results of variance analysis of experimental data, the type of bone, i.e., factor B has the most substantial effect on ultrasound velocity (68.5%, $P<0.00001$). Experimental conditions, or factor A, had a reliable effect (6.7%, $P<0.0001$). The combined effect of factors A and B is insignificant, although it is reliable (3.8%, $P<0.02$). Random factors constituted 21.2%.

Table 1.
Arithmetic means of velocity of ultrasound propagation (numerator, m/s) and coefficients of their variation (denominator, %) in different rat bones under different animal upkeep conditions

Rat group	Tested bone				
	femur			tibia	humerus
	animals' age, months				
	2.5	3	6.5	2.5	2.5
1	2066 / 2,8	2594 / 2,2	2184 / 2,5	2384 / 3,7	2142 / 3,7
2		2668 / 2,8			
3		2537 / 4,3			
4	1986 / 2,7		2139 / 3,3	2246 / 5,4	2053 / 4,5
5	2043 / 3,8			2433 / 3,3	2058 / 3,9

Table 1 lists the arithmetic means for velocity of ultrasound and coefficients of variation for 3 types of bones in the 5 experimental groups. Examination of material from animals 2.5 months of age revealed statistically reliable differences between the parameter for the 1st (vivarium control) and 4th (suspension) groups for all 3 types of bones. Differences between the 5th (hypokinesia) and 1st groups were demonstrated only for parameters of the humerus. Hence, suspension (decreased physical load on limb) leads to statistically reliable decline of ultrasound velocity in the tested bones, which is consistent with data in [14], in which higher values were observed for ultrasound velocity in the tibia of officially rated athletes. Since suspension elicited a concurrent decrease in bone calcium concentration, it can be assumed that the decrease in velocity of ultrasound is related expressly to this. Reliable differences in velocity of

ultrasound were found between the 2d (synchronous control) and 3d (flight) groups. The velocity of propagation of ultrasound in the femur postflight and after the recovery period was lower than in the 1st and 2d groups of rats; however, the differences were reliable only for parameters of the 2d group. Since inflight and synchronous control animals were kept under the same conditions and their movements were not restricted, it can be assumed that slower propagation of ultrasound postflight is due to weightlessness.

Table 2. Thickness of diaphysis wall and calcium content of rat femur without functional load

Animal group	Age, months	Thickness of cortical layer on both sides, mm	Calcium content, g%		
			proximal epiphysis	distal epiphysis	diaphysis
1	2,5	1,02±0,02	23,93±0,55	21,79±0,59	27,03±0,50
4	2,5	0,73±0,01*	21,86±0,64*	18,06±0,45*	26,36±0,41
5	2,5	0,91±0,02*	21,73±0,54*	21,79±0,59*	27,00±0,50
1	6,5	1,75±0,01	21,86±0,43	21,73±0,73	23,46±0,80
4	6,5	1,56±0,01*	23,26±0,82*	19,80±0,29*	23,66±0,43

* $P<0,05$.

Analysis of age-related distinctions of ultrasound conduction in bone revealed that the velocity of ultrasound in the femur increases with increase in age of the rats. The differences between the ages considered were statistically reliable ($P<0.0001$). Typically, 2-5-month animals presented statistically reliable differences between parameters for the 1st and 4th groups, whereas at the age of 6.5 months no such reliability was established. It can be assumed that the bone tissue of young animals is more sensitive to changes in functional conditions of the body than adult animals.

According to the results of correlation and regression analysis, the relationship between ultrasound velocity (see Table 1) and calcium concentration (Table 2) in bones of 6.5-month rats that were suspended can be reliably described by the following equation:

$$C_{sus}^{6.5} = 2291 - 6.81 \cdot Ca_1 + 10.03 \cdot Ca_2 - 11.88 \cdot Ca_3 \text{ (in m/s)},$$

where $C_{sus}^{6.5}$ is velocity of ultrasound in bones of 6.5-month rats (superscript) submitted to suspension (subscript). The standard deviation of regression equation S_R is 50.2 m/s, coefficient of correlation is $R = 0.72$ ($P<0.02$) and coefficient of determination is $D_R = 0.52$. The latter means that 52% of total variance of ultrasound velocity depends on tissue calcium content. Diaphyseal calcium content (Ca_2; see Table 2) has the strongest influence on $C_{sus}^{6.5}$. With increase in calcium content of this part of the bone there is increase in velocity of ultrasound. The specific influence of Ca_2 on $C_{sus}^{6.5}$ constitutes 27.4% ($P<0.04$). In contrast, an increase in calcium content of the proximal epiphysis leads to reduction of ultrasound velocity (specific influence 21.8%, $P<0.05$).

If we consider the joint effect on ultrasound velocity of experimental conditions (control, suspension and hypokinesia) and thickness of diaphyseal wall (2b), the latter will be found to have a reliable effect on velocity of ultrasound (15.3%):

$$C^{2.5}_{\substack{\text{contr.+}\\ \text{sus.+}\\ \text{hypok.}}} = 1763 + 6.2 \cdot Ca_1 - 1.73 \cdot Ca_2 + 199.5 \cdot 2b \text{ (in m/s)}$$

(S_R = 74.1; $P<0.01$; R = 0.47; D_R = 0.22).

When we considered the joint effect on ultrasound velocity of concentration of calcium and thickness of diaphyseal walls, we found, in 6.5-month rats suspended on the stand, that the thickness of walls of the diaphysis had no significant effect on the result:

$$C^{6.5}_{sus} = 2318 - 6.79 \cdot Ca_1 + 9.77 \cdot Ca_2 - 10.76 \cdot Ca_3 - 27.7 \cdot 2b \text{ (in m/s)}$$

(S_R = 52.9 m/s; R = 0.72; $P<0.03$; D_R = 0.52). According to the analysis, Ca_1 has a negative specific influence on value of $C^{6.5}_{sus}$ (21.7%; $P<0.05$) and Ca_2 has a positive influence (26.7%, $P<0.05$).

The relationship between rate of propagation of ultrasound in rat bones at the age of 2.5 months, when the animals were submitted to hypokinesia, and calcium content, as well as thickness of diaphyseal wall, is reliably described by the following equation:

$$C^{2.5}_{hyp} = 2395 - 28.43 \cdot Ca_1 + 11.48 \cdot Ca_2 - 25.62 \cdot Ca_3 + 518 \cdot 2b \text{ (in m/s)}$$

(S_R = 54.3 m/s; R = 0.86; $P<0.05$; D_R = 0.73).

The results indicate that this equation describes better the relationship between velocity of propagation of ultrasound, on the one hand, and calcium content of tissue and thickness of bone wall, on the other hand, than when the animals are suspended: 73% of total variance of ultrasound velocity depends on tissue calcium content and bone wall thickness. Under hypokinetic conditions with 2.5-month rats, there are reliable relations ($P<0.05$) between $C^{2.5}_{hyp}$ and Ca_1 and Ca_3: with increase in calcium concentration velocity of ultrasound diminishes (specific influence constitutes 22.0 and 38.3%, respectively).

The results of the analyses revealed that the effect of calcium concentration on velocity of ultrasound differs in different parts of the bone, which could be due to structural heterogeneity of different parts of bone, and this must be taken into consideration when developing a method of ultrasound diagnosis for bone tissue.

We were also impressed by the fact that ultrasound spread much faster in the tibia than in the femur and humerus. At the same time, according to in vitro studies, the human tibia is heterogenous in velocity of propagation of ultrasound [15-17]. The velocity and logarithmic decrement of ultrasound extinction and value of dynamic modulus of elasticity of bone tissue change in accordance with a person's age [18, 19] and amounts of biochemical substances in tissue [20], in particular calcium and glycosaminoglycans. The high

velocity of ultrasound in the tibia is apparently related to the relatively larger share of compact substance in it. This assumption is confirmed by the fact that when ultrasound was passed only through the diaphyses, the velocity of its propagation was even higher.

It should be noted that the findings obtained by different authors are often dissimilar: some report decline of parameters of mechanical properties of bones under hypokinetic conditions, while others find an increase or absence of changes in the same characteristics. Such contradictions could be attributed to flaws in methods of investigation, as well as failure to consider the effects of biological and nonbiological factors on the results of investigations [17]. There have been few studies of the link between acoustical and mechanical properties of bones [21-23] due to the lack of a sufficient set of research data. It can be assumed that, after the necessary material is collected and the technique for taking measurements is refined, ultrasonic diagnostic methods will make it possible to reliably monitor changes in carrying capacity of bones during long-term spaceflights.

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UDC: 616-001.12-07:616.74-073.432.19-092.9

ULTRASONOGRAPHY OF CANINE SOFT TISSUES DURING DECOMPRESSION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 3, May-Jun 84 (manuscript received 3 Jan 83) pp 52-57

[Article by V. P. Nikolayev, V. P. Katuntsev, R. T. Kazakova, K. S. Yurova, T. D. Doronina, A. D. Mansfel'd, P. K. Chichagov and A. M. Reyman]

[English abstract from source] Ultrasonic location of femoral soft tissues of anesthetized dogs was performed using a modified unit UZKAP-3. The animals were exposed to 0.5 mPa for 2 hours and then to decompression to sea level pressure. The concomitant echographic changes pointed to the formation of extra- and intravascular gas bubbles in the above tissues. The bubbles could be identified visually in the nearest echographic band because the instrumentation used made it possible to eliminate the background image of structural inhomogeneities of the tissue layer.

[Text] Further improvement of objective diagnostic methods and means of preventing caisson's disease in man depends largely on successful development of methods of detecting and quantitative measurement of gas bubbles (GB) that are formed in blood and tissues. The ultrasonographic instruments developed to date, including echocardiographs, permit detection of both moving and stationary GB in the body. Unlike Dopplerian ultrasonic apparatus [1-3], which is suitable for detection only of relatively large GB (over 50 μm in diameter), moving together with blood, this type of instruments is capable of detecting GB of considerably smaller size [4, 5] and showing their exact location. However, the image of GB obtained on echograms made using standard equipment is obscured by the image of structural elements of tissues surrounding them. For this reason, identification of GB on echograms by traditional methods [4, 5] often raises questions as to its reliability.

Our modification of the series-produced ultrasonic echocardiograph UZKAR-3 by adding to its circuit a system of automatic timed control of amplification (ATCA) and use of an ultrasonic sensor with spatially separated transmitting and receiving piezoelectric transducers makes it possible to simplify appreciably the detection of GB in tissues and vessels situated in the near zone of location. Previously, this instrument was used to record penetration of GB into the aorta of anesthetized and thoracotomied dogs during intravenous infusion of air. On the echograms we obtained, the images of GB in the pulmonary artery and aorta were not obscured by images of structural elements of the walls of these vessels [6].

Our objective here was to check whether it is possible to use the modified UZKAR-3 instrument for detection of GB in soft tissues of animals submitted to decompression from high pressure to pressure on the ground.

Methods

In our experiments, we used 15 mongrel dogs of both sexes weighing 9.1-20 kg. EKG electrodes and a carbon sensor to pick up respiration rate were applied to the animal, anesthetized with nembutal (70 mg/kg) and immobilized in supine position. The ultrasonic sensor, swabbed with sound-conducting paste, was applied to the shaved surface of the soft part of the thigh of the hind limb and secured with a rubber bandage. The animal was then placed in an RKM-2 pressure chamber and, after connecting the EKG and respiration sensors through the electric outlets in the chamber to an RM-150 Nihon Kohden polygraph, and the ultrasound sensor to the modified UZKAR-3 instrument, we performed compression delivering compressed air to a pressure of 0.5 mPa at the rate of 0.1 mPa/min. The animal was kept at this pressure for 2 h, after which it was decompressed to ground pressure (0.1 mPa) at the rate of 0.1 mPa/min. We assessed the animal's condition at all stages of the experiment on the basis of the EKG and respiration curves recorded automatically and displayed on the oscilloscope of the RM-150 polygraph, while the echogram of the probed part of the thigh was viewed on the screen of the monitoring oscilloscope of the UZKAR-3 instrument, taking periodic photos from the screen of another oscilloscope with a Zenith-E camera.

The specifics of operation of the ATCA system, which we added to the circuit of UZKAR-3 can be graphically seen by comparing echograms 1a and 1b, which were obtained upon probing the soft tissue of the thigh of one of the animals at the start of the experiment. The distance between adjacent markers vertically corresponds to 1 cm probing depth and horizontally to a time interval of 0.5 s. The location on the echograms of the surface of the sensor (SS) adjacent to the surface of the probed tissue is marked on the left by the SS level. It was established at first on an echogram reflecting the movement of a metal plate toward and away from the surface of the sensor placed in water. Echogram 1a, which was obtained with the instrument operating in the standard mode, between the SS level and second line from the top, which shows the location of the sensor of the receiving piezoelectric transducer submerged in the body, illustrates the echosignals from heterogeneities in structure of the body of the sensor. The same echosignals, rereflected from the sensor surface are also shown below the SS level, together with echosignals from structural elements in the probed tissue. Echogram 1b was obtained with the instrument operating in the mode of triggered ATCA system, which attenuates the sensitivity of the receiver for the close echosignals. Figure 1b shows that the ATCA system permits elimination of the image of heterogeneities of the body of the sensor and structural elements of the tissue layer in the near-zone of location.

For each animal, on the initial echogram of the 1b type, we eliminated the image of structural elements of the tissue layer 1.0-1.5 cm in thickness that was closest to the sensor, and with the instrument operating in the same mode, we observed and photographed echograms at all subsequent stages of the experiment. We determined from the location and intrinsic features of the reference

image of tissue structures in the far range of location whether contact was retained between the sensor and the animal's body and chosen direction of location remained unchanged. Appearance of visible echosignals in the course of the experiment in the closest band of the echogram, which was initially dark, was interpreted as appearance of GB in the corresponding layer of tissue. We stopped the observations and photography 1.5 h after termination of decompression.

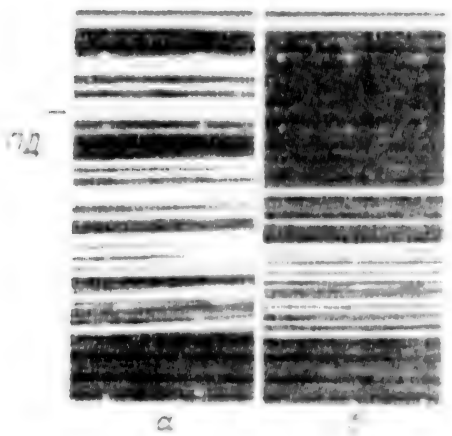


Figure 1.
Effect of ATCA system on appearance of soft tissue echogram
a) with operation of UZKAR-3 instrument in standard mode
b) with operation of ATCA system
ПД) location of sensor surface [SS]

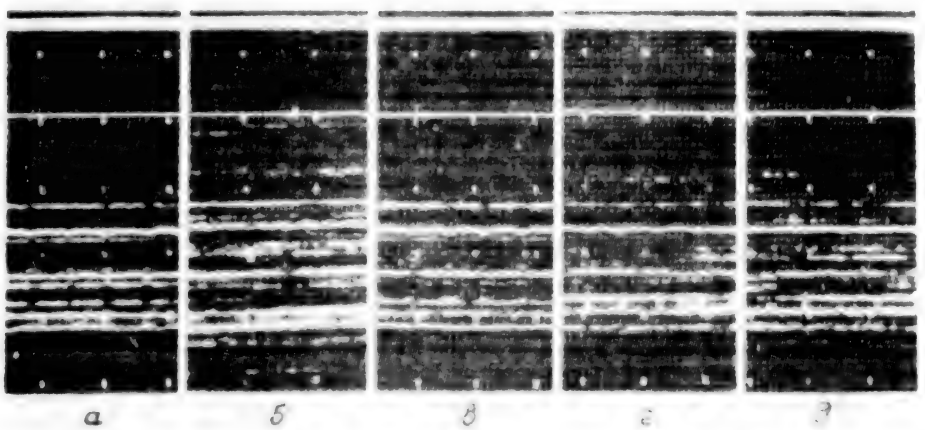


Figure 2. Changes in echogram of canine femoral soft tissue in the course of the experiment

а) before and during compression, during 2-h exposure of animal to pressure of 0.5 mPa, as well as during decompression and for some time after it
б-д) 9, 12, 14 and 63 min after termination of decompression

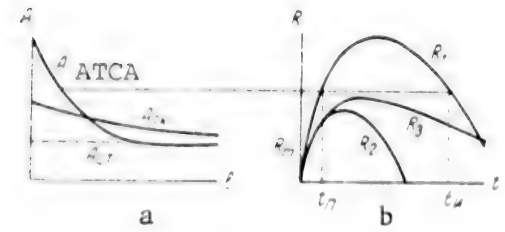
Results and Discussion

In the course of the experiment, visible echosignals appeared in the near band of the thigh tissue echogram in 3 out of 15 animals. The order of changes in the echogram of one of these 3 animals is illustrated in Figure 2. The second line from the top on the echograms (see Figure 2*а*-2*д*) shows the location of the surface of probed tissue. In this experiment, we created its image deliberately by removing contact paste from a small part of the sensor surface, beyond which was located the emitting ultrasonic piezoelectric transducer. The operating mode of the modified UZKAR-3 instrument was selected in such a manner as to have no image of structural elements of the layer of tissue, 1.2 cm thick, closest to the sensor on the initial echogram (see Figure 2*а*). The echogram of probed tissue retained the appearance illustrated in Figure 2*а* during compression, the 2-h exposure of the animal to a pressure of 0.5 mPa, as well as during decompression and for some time after it.

The first signs of GB in the tissue layer closest to the sensor became noticeable about 9 min after decompression. For a short time (2-3 min), the echosignals from them were unstable (see Figure 2*б*). Then a stable image appeared of one GB (see Figure 2*в*) and 2 min later, of another (see Figure 2*г*). However, about 1 h after decompression, the echographic images of these GB, which were 0.4 and 1.0 cm away from the surface of the sensor, became unstable for a brief time (see Figure 2*д*) and soon disappeared entirely. In two other animals, there was analogous appearance and disappearance in the course of the experiment of GB images in the near band of the echogram.

As can be seen by comparing Figure 2*а* and 2*б*-2*д*, after decompression the echogram of the layer of tissue more than 1.2 cm away from the tissue surface also underwent a change. The previously visible lines in the far band of the echogram remained in their former place, but at times they became brighter and wider than initially. Moreover, new lines were added to them, the width and brightness of which also varied in the course of the experiment. We observed such changes in the far band of the echogram of femoral tissue in all 15 animals, and apparently they were due to appearance of GB in the corresponding layer of tissue. A difference between the far band of the echogram and the initial appearance usually occurred before appearance of visible echosignals in the near band of the echograms, and in some cases it did not disappear to the end of the experiment. However, it should be noted that some doubt arises upon visual identification of GB in the distant layer of tissue according to changes in appearance of the corresponding echogram band.

In our experiments, the animals were submitted to decompression that inevitably caused GB production in the vascular stream. This was indicated by the profusion of GB visible to the eye in samples of venous blood, which we drew from the right ventricle of some animals to determine gas composition of blood. In addition, after decompression all animals developed overt dyspnea and their heart rate increased, which was also indicative of development of vascular gas embolism. However, in view of the absence of objective and unequivocal signs of formation of extravascular and intravascular GB during decompression, we can only discuss tentatively the onset of this phenomenon in some specific tissues. For this reason, additional validation is required to equate the postdecompression changes in the soft tissue echogram, which we observed, with appearance of GB in it.



a b

Figure 3.
Conditions for detection of gas bubbles in soft tissues

a) qualitative operating characteristics of modified UZKAR-3 instrument
ℓ) probing depth
A) amplitude of echosignals
A_{TK}) maximum amplitude of echosignals from structural tissue heterogeneities
A_{CT} and A_{ATCA}) minimum amplitude of echosignals detected by instrument when it operates in standard mode and with operation of ATCA system
b) qualitative appearance of evolution of bubbles formed in tissue after decompression and remaining in situ--time after termination of decompression
R) radius of bubble
R_1, R_2, R_3) possible curves of growth and resorption of bubbles
R_m) minimum size of bubbles distinguishable by instrument in distant probing zone
$t_п$, $t_и$) time of appearance and disappearance of images of type R_1 bubbles in middle of initially dark echogram band*

Figure 3 illustrates the conditions for detection of GB in tissue with the help of the ultrasonic echographic equipment we used. Echosignals from structural heterogeneities of tissue vary in amplitude, and its maximum value for each level of intensity of probing ultrasound changes as a function of depth of probing in accordance with a curve of the A_{TK} type, shown in Figure 3a. The decrease in amplitude of echosignals from the distant probing zone is due to absorption and scatter in tissue of the emitted and reflected ultrasound. When the UZKAR-3 instrument operates in the standard mode, the amplifier of the receiver and signal intercept system are adjusted so as to reflect on the oscilloscope screen only the echosignal with amplitudes in excess of the A_{CT} level.* The ATCA system which we added to the instrument lowers sensitivity of the receiver exponentially for close echosignals but retains it at the former level for distant echosignals. By adjusting the ATCA, one can set an operating mode for the instrument, in which the minimal amplitude of echosignals shown on the oscilloscope changes with change in depth of probing, in accordance with a curve of the A_{ATCA} type illustrated in Figure 3a. In the near-zone of location, this curve is above curve A_{TK}, which is what eliminates the sonographic images of structural heterogeneities in the corresponding layer of tissue.

The animal tissue areas we tested were isotropic in relation to ultrasound. This is indicated by the fact that the width of the dark echogram band set at the start of the experiment remained unchanged during longitudinal and angular scanning of the animal's thigh (when shifting the sensor over the shaved surface of the thigh and turning the sensor applied to it about an axis perpendicular to the probing direction). In some experiments, with the instrument operating continuously, the near and far bands of the echogram retained their initial appearance for 4 h (from the time the sensor was placed to the end of decompression), which is indicative of stability of instrument characteristics and, in particular,

Translator's note: Subscripts represent Russian words for tissue, standard mode, appearance and disappearance of bubble images.

unchanged mutual location of curves A_{TK} and A_{ATCA}, as well as absence of any changes in tissue structure under the influence of ultrasound.

In the light of these facts, appearance after decompression of visible echosignals in the initially dark band of the echogram signifies appearance of structures in the corresponding tissue layer that have high reflection capacity. Since it is unlikely that there are any mechanisms for "consolidation" of tissue structures under the effect of decompression, it is logical to assume that the sources of these strong (with amplitude in excess of A_{ATCA}) echosignals were GB, which were formed in the tissue layer closest to the sensor or carried there from adjacent regions. The change in the far band of the echogram was also due to appearance of GB in the corresponding tissue layer.

The specifics of postdecompression appearance of new echosignals and their subsequent disappearance correlated quite well with the theoretically assumed process of growth and resorption of GB formed in body tissues and remaining there in situ. The inherent distinctions of this process can be represented in a mathematical model [7], which describes the exchange of inert gas between tissues and blood together with evolution of GB in them. According to this model, Figure 3b illustrates in qualitative form the possible growth and subsequent resorption of individual GB in tissue of homogeneous consistency provided they were formed at the moment of termination of decompression. In tissue of such a type that is uniformly saturated with inert gas, the causes of differences in maximum size and lifespan of GB are differences in volume of tissue segments from which they take gas for their growth, as well as differences in blood supply to these segments. For example, it can be considered that GB of the R_1 and R_2 type differ from one another for the first of the above reasons, while types R_2 and R_3 differ for the second one. If, however, tissue is heterogeneous in consistency and unevenly saturated with inert gas, the differences in evolution of individual GB in it may be due to a difference in many factors that influence the course of this process.

The amplitude of echosignals from GB is proportionate to their radius, and for this reason a comparison of curve A_{ATCA} in Figure 3a to the type R_1, R_2 and R_3 curves in Figure 3b, which characterize GB evolution, enables us to judge the relative dimensions and time of detection of GB at different depths of scanned tissue. Thus, in the middle of the initially dark echogram band, echosignals can be recorded only from relatively large GB of the R_1 type. In the far probing zone, the instrument is capable of detecting not only large, but smaller GB of the R_2 and R_3 types. However, in this locating zone, the minimal size of GB detectable with the instrument must be somewhat larger than R_m shown arbitrarily in Figure 3b, since the amplitude of echosignals from GB diminishes as they move away from the surface of the sensor due to absorption and scatter of ultrasound in tissue. Time of appearance ($t_П$) and subsequent disappearance ($t_И$) of echographic images of GB are determined by both the rate of their growth and resorption, and sensitivity of the instrument's receiver. Because of the differences in receiver sensitivity to near and far echosignals produced by the ATCA system, the images of synchronously growing GB at different scanning depths appear at different times. They become visible later in the tissue layer closest to the sensor than in the distant layer.

At the same time, not only isolated in situ GB could be the source of new echosignals visible on the oscilloscope after decompression. It is quite

possible that, in our experiments, these echosignals originated from both isolated extravascular or intravascular GB brought to the probed tissue area from adjacent ones, or that they were the result of summation of weak echosignals from small GB undetectable individually by the instrument and at about the same distance from the sensor, as well as structural heterogeneities of tissue. The effect of summation of echosignals from several objects reflecting ultrasound depends largely on their reciprocal location. For this reason, when there is a minor change in location of individual small GB or when they move with the flow of blood or lymph, the amplitude of the composite echosignal should undergo significant fluctuations, which is apparently one of the causes of instability of some elements of the echogram. The images of flow of GB in blood vessels that are detectable by the instrument, as well as images of isolated in situ GB near the lateral margins of the probed tissue area, could also be unstable.

Thus, the results of this study and our previous ones [6] confirm the possibility of using the modified UZKAR-3 instrument for detection and recording extravascular and intravascular GB formed in body tissues during decompression. However, the simplicity and unequivocal nature of GB identification in a tissue layer and vessels situated in the near zone of location provided by the ATCA system are obtained at the price of lowering the sensitivity of the instrument's receiver to close echosignals, and for this reason only relatively large GB can be detected in this zone. Judging by the changes in the distant band of the echogram after decompression, formation of GB of their passage into the probed tissue of the thigh from elsewhere occurred in all animals, but an unobscured image of GB in the near band of the echogram, which was initially dark, was seen in only 20% of the animals. The absence of GB in the nearest layer of tissue that could be detected by the instrument in the rest of the animals was apparently due to inadequate saturation of the body due to anesthesia during the 2-h exposure to 0.5 mPa pressure or excessive increase in receiver sensitivity to the closest echosignals. Special investigations are required to determine the smallest size of GB that can be detected and unequivocally identified by the instrument in the near-zone as a function of power of emitted ultrasound, general amplification of the receiver, level of echosignal intercept and adjustment of ATCA.

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FUNCTIONAL STATE AND WORK CAPACITY OF MAN WHEN BREATHING OXYGEN AND HYPOXIC MIXTURES UNDER POSITIVE PRESSURE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 3, May-Jun 84 (manuscript received 15 Jul 83) pp 57-60

[Article by M. D. Draguzya, V. I. Kopanev and S. I. Lustin]

[English abstract from source] Experiments were carried out at sea level to investigate tolerance and work capacity of test subjects breathing 100% oxygen and hypoxic gas mixtures (HGM) containing 12.7-12.8% O_2 at a positive pressure of 800 mm H_2O. All test subjects tolerated 1 hour exposure to 100% O_2 or HGM under positive pressure. However, HGM induced more distinct cardiopulmonary changes than O_2. During the first minutes of exposure to positive pressure breathing the tracking performance deteriorated most. The number of errors was 24.5% with O_2 and 21.4% with HGM more than in the pretest study. As the adaptation developed, the number of tracking errors decreased to reach the pretest level with O_2 and to remain 6-10% higher than the pretest level with HGM.

[Text] Accidental depressurization of aircraft cabins may occur during stratospheric flights. As we know, in such cases oxygen is delivered to the pilot's airways at positive pressure (PP). PP breathing causes considerable strain on physiological functions of a number of organs and systems of the body. In this regard, it is assumed that, after cabin depressurization, a pilot should immediately descend to a safe altitude. However, in some situations this cannot always be done.

Pure O_2 was used in a number of studies of human tolerance of PP breathing on the ground as related to conditions of aircraft cabin depressurization at altitudes in excess of 12,000 m. Unfortunately, this methodological procedure is not without flaws. It does not fully simulate actual conditions of oxygen delivery to a pilot, since he would experience some hypoxia with depressurization of the cabin at the above altitudes, even when using oxygen gear, if absolute oxygen pressure in his helmet does not exceed 145 mm Hg [1]. Yet the use of pure O_2 for PP breathing on the ground leads to hyperoxia.

In view of the foregoing, our objective here was to test under ground-based conditions the effect of long-term PP breathing using pure O_2 and hypoxic gas

mixtures (HGM), which simulated the conditions of oxygen delivery in case of cabin depressurization in the stratosphere, on man's functional state and work capacity.

Methods

Two series of 15 test were conducted on the ground with the participation of 15 volunteer subjects 18-27 years of age. PP of 800 mm water was created by means of an oxygen training instrument in 3-4 s. External compensation was obtained by using a pressure suit and pressure helmet. PP breathing lasted 1 h. In the first series, the subjects breathed pure O_2 and in the second, hypoxic mixtures containing 12.7-12.8% O_2, which were equivalent to PP breathing O_2 at altitudes of about 15,000 m according to partial oxygen tension they created in alveolar air when breathing at PP of 800 mm water. We used a unit for two-dimensional compensatory tracking to test work capacity. Testing time was arbitrarily divided into 15-min cycles. In each cycle, the subjects had to perform two-dimensional compensatory tracking of banking and pitching (the pointers on the control ["director"] instrument moved according to the sinusoidal law) for the first 3 min. Performance was evaluated according to mean integral tracking error in relative units. In the remaining time of each 15-min cycle, we recorded heart rate (HR), respiration rate (RR), voluntary breath-holding time in inspiration, hand dynamometry and effected visual observation. We recorded synchronously the EKG, rheogram of the right lung and acceleration kinetocardiogram from the zone of projection of the right ventricle for analysis of hemodynamics in the pulmonary circulation [2, 3]. Mechanical systole time, periods of contraction and expulsion, phase of isometric relaxation of the right ventricle were determined from the kinetocardiogram. Knowing the duration of the phase of isometric relaxation, we calculated systolic pressure in the pulmonary artery using the formula proposed by A. A. Popov [4]. We determined the rheographic and dicrotic indexes, as well as amplitude and frequency indicator, from the data on the rheogram. The obtained material was submitted to statistical processing on an MIR-2 computer. The T criterion was determined by the difference method.

Results and Discussion

The results of our tests established that breathing at PP of 800 mm water, using both pure O_2 and HGM for 1 h, was tolerated by all subjects. The complaints in common in both the first and second series were discomfort, suit pressure on the body and, occasionally, numbness of the lower limbs. These signs were observed for the first 5-10 min of PP breathing. Thereafter, the subjects adapted to the test conditions and observed no unpleasant sensations. When breathing HGM, there was a change in the appearance of the subjects: their faces turned pale and hands became cyanotic, which was not observed when using O_2.

As can be seen in Table 1, HGM breathing led to a greater functional load on the cardiovascular and respiratory systems than O_2. With use of pure O_2, we observed insignificant but reliably slowing of HR and reliable increase in breath-holding time. With HGM, these reactions were in the opposite direction, i.e., increase in HR and decrease in breath-holding time. This shows that, at the PP level used, the oxygen budget of the body was apparently the main factor determining its state.

Table 1. Dynamics of physiological parameters when breathing O_2 and HGM at PP of 800 mm water (M±m)

Stage of study	Pure O_2 breathing				HGM breathing			
	HR per min	RR per min	dynamometry kg	breath-holding s	HR per min	RR per min	dynamometry kg	breath holding s
Background	68.5±2.2	14,5±0,6	55,1±1,3	64,5±2,8	66,4±1,5	14,8±0,5	53,2±1,2	67,7±3,9
PP 800 mm water:								
0-15 min	68,8±1,8	14,7±0,6	52,3±1,3***	63,6±4,6	76,8±1,8***	17,2±0,5***	49,8±0,9**	29,6±1,7***
16-30 min	66,4±1,9	15,3±0,5	50,1±1,2***	73,8±4,9*	77,6±2,1***	17,6±0,4***	47,3±1,0***	34,1±2,4***
31-45 min	64,5±1,9**	15,2±0,5	48,5±1,3***	83,1±4,7***	76,0±1,6***	18,8±0,5***	45,6±1,0***	30,8±1,2***
46-60 min	68,3±1,8	15,6±0,6*	47,3±1,3***	82,3±4,9***	77,2±1,7***	19,1±0,5***	44,7±1,1***	30,6±2,1***
After PP	67,3±2,5	15,3±0,6*	50,7±1,2***	63,2±3,7	63,6±1,5**	15,3±0,4	50,3±0,7**	71,0±3,7

Note: Here and in Table 2: *P<0.05 in relation to background, **P<0.01 ***P<0.001

Table 2. Dynamics of indicators of phase structure of right ventricular cycle and systolic pressure in pulmonary artery when breathing O_2 and HGM at PP of 800 mm water (M±m)

Stage of study	Pure O_2 breathing				HGM breathing			
	tension period, s	expulsion period, s	mechanical systole, s	systolic pressure in pulm.artery mm Hg	tension period, s	expulsion period, s	mechanical systole, s	systolic pressure in pulm.artery mm Hg
Background	0,1±0,004	0,301±0,003	0,335±0,004	34±2,7	0,1±0,005	0,313±0,005	0,344±0,004	23,3±1,7
PP 800 mm water:								
0-15 min	0,09±0,005*	0,309±0,005	0,333±0,007	31±2,7	0,092±0,004*	0,301±0,006*	0,333±0,005*	27,8±3,2
16-30 min	0,075±0,08*	0,304±0,005	0,337±0,005	27±3,0	0,087±0,003*	0,296±0,006**	0,327±0,007**	38,9±3,5**
31-60 min	0,088±0,004*	0,303±0,004	0,337±0,004	28±2,5	0,089±0,004*	0,296±0,006**	0,328±0,007*	37,8±3,6**
After PP	0,09±0,003	0,301±0,006	0,331±0,007	29±3,1	0,094±0,003	0,323±0,004**	0,356±0,004*	23,1±1,1
10 min after PP	0,098±0,002	0,303±0,003	0,336±0,005	31±3,1	0,098±0,004	0,318±0,005	0,350±0,004	24,4±1,8

The gradual decline of dynamometry was indicative of decreased force of hand flexors, which was observed to a greater degree when using HGM for breathing. In essence, this can be related to impaired contractility of muscle tissue due to general local circulatory disorder as a result of compression of the limbs in the compensating suit and development of tissular hypoxia, which is more marked when using HGM.

Table 2 lists data characterizing the dynamics of indicators of phase structure of the cardiac cycle. As can be seen in this table, when breathing pure O_2, there was reduction of tension period. The period of expulsion and mechanical systole showed a tendency toward insignificant increase. Under the same conditions, HGM breathing led to reduction of tension period, as well as expulsion period and mechanical systole. A comparison of expulsion period and mechanical systole at different stages of the study to their nominal values, calculated with the formulas proposed by I. Ye. Oranskiy [3], revealed that the difference did not exceed 0.006 s when using either O_2 or HGM. Consequently, the contractility of the right ventricular myocardium remained at a rather high level in the first and second series of tests. However, use of HGM led to more marked structural changes in right heart function.

Systolic pressure in the pulmonary artery, which was calculated from the phase of isometric relaxation, had a tendency toward dropping with O_2 breathing, whereas with HGM it gradually rose, with increase in duration of PP breathing.

The rheographic data indicated that PP breathing led to decrease in pulsed delivery of blood to the lungs and increase in peripheral resistance in the pulmonary circulation. This is related to stretching, elongation and compression of capillaries with stretching of pulmonary alveoli [5]. The more labored blood flow in the pulmonary circulation, against the background of more intensive cardiac function due to hypoxia under the effect of HGM breathing, apparently was the cause of pressure elevation in the system of the pulmonary artery.

Analysis of work capacity in the tracking test revealed that the largest number of errors were made in the first min of PP breathing, in both the first and second series of studies. In this period, the increment of integral errors constituted 24.5% in relation to base data with O_2 breathing and 21.4% with HGM. Thereafter, the number of errors diminished and, by the end of the test in the first series, reached the base level, whereas in the second series it exceeded the latter by 6-10% and reverted to base data only after removal of PP. Such a pattern of change in work capacity when breathing pure oxygen at PP was reported elsewhere [6, 7]. Our findings indicate that PP plays the leading role in impairing work capacity during the first minutes of PP breathing, since the initial increase in errors was the same with use of both O_2 and HGM. However, later on, as the body adapted to PP, the hypoxia that developed prevented complete restoration of quality of tracking performance.

Thus, the results of these studies indicate that, breathing HGM, as compared to O_2 under PP elicits more significant functional changes in the body and leads to worsening of quality of tracking performance.

In case of aircraft cabin depressurization at altitudes where O_2 is delivered at PP of 800 mm water, the pilot using oxygen gear operating in the mode of

absolute pressure of 145 mm Hg underneath the helmet disposes of considerable spare time. True, his work capacity diminishes somewhat.

Under ground-based conditions, during psychophysiological training of pilots for situations with depressurization of the aircraft cabin at altitudes in excess of 12,000 m, it is desirable to use HGM, rather than pure O_2, for PP breathing, which is equivalent to breathing pure O_2 under PP corresponding to a specific altitude according to the partial O_2 tension they create in alveolar air.

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UDC: 612.45+612.826.4+612.432]-06:
[612.273.2+612.592

ADRENAL-HYPOTHALAMUS-PITUITARY SYSTEM REACTIONS IN RATS COOLED IN A HYPOXIC-HYPERCAPNIC GAS ATMOSPHERE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 3, May-Jun 84 (manuscript received 19 Oct 82) pp 61-65

[Article by S. S. Mogutov, Ye. S. Sergeyeva and V. P. Yevgraf'yev]

[English abstract from source] The rearrangement of the adrenal-hypothalamus-pituitary system of rats kept in a low-temperature hypoxic-hypercapnic atmosphere was investigated. Phasic changes of the system were detected, with their magnitude and sign depending on the exposure time. The central and peripheral components of the system developed specific relations. One of the peculiarities of the responses of the adrenal-hypophysis-pituitary [sic] system to the above exposure is a limited range of changes in the neuroendocrine activities due to a total reactivity decrease. This protects the neuroendocrine system from overstrain or involvement in overshooting reactions. It is assumed that this type of response of the adrenal-hypophysis-pituitary [sic] system is important to help understand mechanisms of the neuroendocrine regulation of the adaptive process developing in response to the combined effect.

[Text] Several studies have demonstrated that the combined effect on rats of low temperature and hypoxic-hypercapnic atmosphere is enhancement of resistance of experimental animals to profound and prolonged hypothermia, as well as acute ischemia of the brain [1-3]. However, the pathophysiological mechanisms of the adaptive process leading to increased resistance in interaction of altered gas environment and temperature factors have not been sufficiently investigated. In particular, in spite of the significance that is attributed to the hypothalamus-pituitary-adrenal system in formation of resistance [4-8], there are virtually no data in the literature available to us concerning the distinctions of the reaction of this part of the neuroendocrine system on cooling of animals under hypoxic and hypercapnic conditions. The few studies that have been conducted, using morphological and histochemical methods of assessing the functional state of the adrenals, hypothalamus and hypophysis exposed to the combined factors, did not provide adequate clarity to this matter [2]. For this reason, we investigated here the dynamics of functional state of the adrenal-hypothalamus-pituitary system of rats when they are cooled in an altered gas atmosphere and in the recovery period after such exposure.

Methods

Experiments were performed on 230 mongrel male rats weighing 180-200 g at the same time of day in the fall and winter. We used the method of Giaja and Andjus [1, 9] to cool the rats under hypoxic and hypercapnic conditions. Specimens were taken (hypothalamus, adrenals, blood) after decapitating the rats, in the 20th, 50th, 70th, 90th, 120th min from the start of exposure, then 3 and 48 h after its termination. We measured percentage of O_2 and CO_2 in the pressure chamber, and we recorded the animals' rectal temperature.

To evaluate functional changes in the adrenal cortex and pituitary gland we used fluorimetric assay of 11-hydroxycorticosteroids (11-HCS) in blood and tissue of the adrenals by the method of deMoor et al. [10] as modified by V. V. Davydov [11] and the radioimmunological method for assaying blood plasma adrenocorticotropic hormone (ACTH) using standard sets of the Amersham firm (England).

The brain was fixed in Bouin fluid to determine the level of activity of anterior hypothalamic neurosecretory cells (NSC). Paraffin sections were stained according to Gomori-(Gab) with additional staining according to Heidenhain or methyelen blue according to V. F. Mayorova [12]. Using a screw-type ocular micrometer (MOV-15) at general magnification of 15× ocular and 90× objective, we measured nucleus and nucleolus volumes in NSC. Volume of nuclei was calculated using the formula for an ellipsoid of rotation:

$$V = \frac{\pi}{6} \cdot D^2$$

and volume of nucleoli according to the formula for a sphere:

$$V = \frac{\pi}{6} \cdot D^3$$

We counted the percentage of different types of NSC as classified arbitrarily by A. L. Polenov [6] in the supraoptical (SON) and paraventricular (PVN) nuclei of the hypothalamus.

The obtained data were submitted to processing by methods of variation statistics with determination of probability of differences using Student's criterion [13].

Results and Discussion

The results of these experiments, which are illustrated in Figure 1, revealed that there was a 184.4% increase in concentration of 11-HCS (from 15.4±0.9 to 43.8±1.8 µg%) of blood plasma within the first 20 min of exposure, as compared to rats in the control group. Corticosteroid content of adrenal tissue did not change appreciably (1457.4±53.9 µg% after 20 min, versus 1370.2±89.9 µg% in the control). ACTH concentration decreased with statisticaly reliability ($P<0.05$; see Figure 1) at this time. Volume of NSC nuclei in the SON and PVN increased, as compared to intact animals, while the size of nuclei diminished ($P<0.05$; Figure 2).

After 15 min, 11-HCS content increased by 1.4 times as compared to 20-min level in plasma and by 2.4 times in the adrenals. Volume of nuclei in the SON did not

change, but continued to increase in the PVN. Nucleolar volume increased in both hypothalamic nuclei, although it did not exceed the volume demonstrated in intact rats (see Figure 2). Unlike the SON, in the PVN we observed an insignificant increase in type I cells with decrease in types II and III cells at this time (Figure 3).

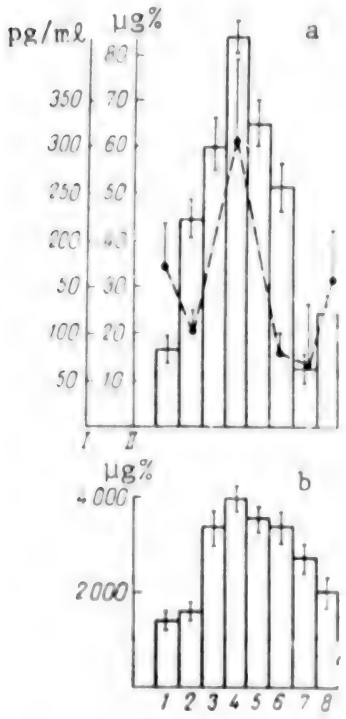

Figure 1.
Effect of cooling hypoxic-hypercapnic rats on levels of 11-HCS (bars), ACTH (dash line) in blood plasma (a) and 11-HCS in adrenals (b)
X-axis, time (1-8--control, 20th, 50th, 70th, 90th and 120th min, respectively, of combined exposure and 3 and 48 h after it).
Y-axis, concentration of ACTH (in pg/mℓ, I) and 11-HCS (μg%, II)

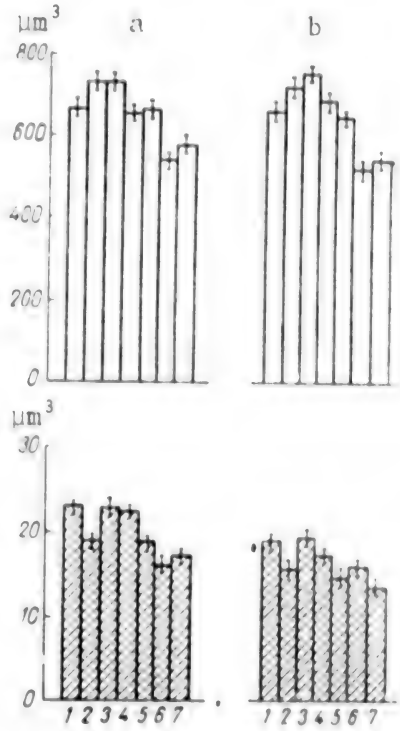

Figure 2.
Effect of cooling hypoxic-hypercapnic rats on size of nuclei (white bars) and nucleoli (crosshatched bars) of anterior hypothalamic NSC
a) SON b) PVN
X-axis, time (1-7, control, 20th, 50th, 70th, 90th, 120th min, respectively, of exposure, and 48 h after it).
Y-axis, volumes of nuclei and nucleoli (μm^3)

Maximum increase in the tested blood plasma and adrenal hormones was observed in the 70th min of cooling (see Figure 1). As compared to the dimensions of NSC nuclei and nucleoli demonstrated after 50 min of exposure, the volume of SON and PVN cell nuclei, as well as of nucleoli in PVN NSC, decreased with statistical reliability ($P<0.05$).

Thereafter (90th min of exposure) plasma and adrenal 11-HCS content diminished reliably ($P<0.05$). There was decrease in volume of NSC nuclei in PVN and nucleoli in SON and PVN ($P<0.05$). At this stage of cooling, there was an

increase in number of type I cells and decrease in types II and III cells. There was the opposite change in proportion of NSC types in the PVN (see Figures 2 and and 3).

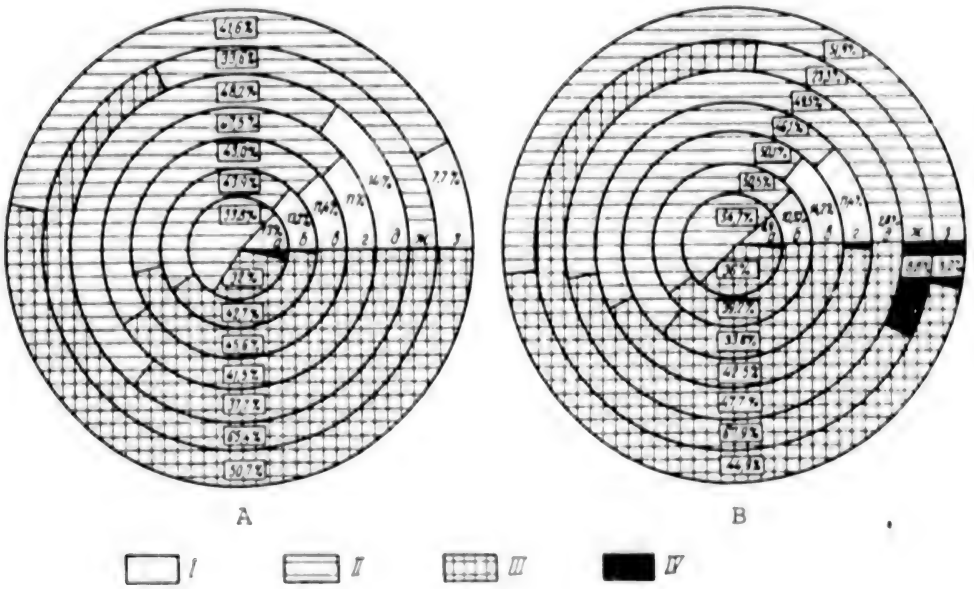

Figure 3. Proportion of different types of neurosecretory cells in nuclei of anterior hypothalamus at different stages of combined exposure

A) supraoptical nucleus
B) paraventricular nucleus
а,б,в,г,д,ж,з) control, 20th, 50th, 70th and 120th min of exposure, and 48 h after it, respectively
I-IV) types I-IV cells, respectively

The numerals in the figure refer to percentage of cells of indicated type.

At the end of the cooling period (120th min), 11-HCS levels in blood and the adrenals continued to decline. We observed marked reduction in volume of cellular structures in nuclei of the anterior hypothalamus and in concentration of ACTH in plasma. Only types II and III cells were demonstrable in the SON and PVN, and the number of type I cells increased to 8.8% in the PVN (see Figure 3).

In the recovery period (3 h after exposure), 11-HCS content of plasma was 1.4 times lower than in intact rats and 2 times higher in the adrenals. ACTH content of blood plasma dropped to 99.4±22.6 pg/mℓ (control 169.0±17.9 pg/mℓ). Concentration of 11-HCS in blood and adrenals 48 h after exposure exceeded the hormone levels demonstrated in the control group of rats. ACTH content did differ reliably from the concentration found in intact rats (see Figure 1). The volumes of nuclei and nucleoli remained low, although there was a tendency toward restoration of proportion of NSC types inherent in control animals, more marked in the SON (see Figures 2 and 3).

Thus, cooling animals under hypoxic and hypercapnic conditions elicited phasic change in functional state of the system in question. Since the volume of

nucleoli is one of the most relevant indicators of intensity of hypothalamic cell neurosecretion [14], there is decrease in SON and PVN activity at the first stage of exposure (20th min). This is in contradiction with our demonstration of enlargement of NSC nuclei. However, several studies have shown that the volume of nuclei and nucleoli does not necessarily change in the same direction. Inhibition of secretion may be associated with enlargement of nuclei in some cases [15]. At the start of exposure, there was depression of adrenocorticotropic function of the adenohypophysis. The increase in 11-HCS content of blood is indicative of increased adrenal activity; however, the insignificant increase in adrenal tissue hormones warrants the assumption that, in this period, processes causing passage of glucocorticoids into blood prevail over their intensified synthesis in the gland. When considering the combined factors as a single stressor stimulus, one must bear in mind that, in the model we used, the animals were submitted to a constantly changing gas atmosphere. For this reason, different correlations developed at each stage between the body and the environment, which determine the nature and extent of functional changes in the system under study.

Changes in rats' rectal temperature, O_2 and CO_2 content in pressure chamber during cooling of animals under hypoxic and hypercapnic conditions

Time after start of exposure, min	Rectal temp. °C	CO_2 content vol%	O_2 content vol%
20	36.0±0.12	6.4±0.3	11.3±0.45
50	31.4±0.1	11.8±0.23	6.6±0.18
70	28.0±0.05	12.1±0.11	4.5±0.12
90	26.0±0.09	13.8±0.28	3.8±0.2
120	20.4±0.03	14.9±0.15	2.5±0.09

At the first stage after 20-min exposure, rat body temperature dropped insignificantly, whereas CO_2 level in the pressure chamber rose to 6.4±0.3 vol% and concentration of O_2 dropped to 11.0±0.05 vol% (see Table). Accordingly, the change in the system under study at this time apparently depends significantly on the hypoxic-hypercapnic component of the combined factor. Several authors have demonstrated that the adrenal reaction is less marked under hypoxic conditions than the response to another type of stress stimulus [16]. It was also established that hypercapnia concomitant with hypoxia diminishes the gland's reaction to a greater extent [17]. Our finding of a diminished adrenal reaction to the combined factors conforms with the results of the cited studies. The results of experiments dealing with changes in central elements of the system warrant the statement that the form of adrenal response at the early stages of exposure to an altered gas atmosphere is attributable to diminished ACT function of the adenohypophysis. Analysis of correlations formed between the anterior lobe of the hypophysis and adrenal cortex, with consideration of data in the literature concerning the role of the anterior hypothalamus in regulation of the adenohypophysis [4, 6, 18, 19], warrant the belief that they are determined by the functional state of the hypothalamus. At the same time, the demonstrated relationship between direction of change in concentration of ACTH and 11-HCS suggests that, when the body is exposed to a hypoxic-hypercapnic gas atmosphere, ACTH is not the only regulator of 11-HCS level in the blood stream, as was demonstrated for hypoxic stress.

At the second stage of the exposure period (50th-70th min), the increase in CO_2 and decrease in O_2 content of inhaled air (see Table) start to have an effect that is in the same direction as the cold factor, influencing intensity of

metabolism [20,21, 22] and blocking heat regulation [23, 25], which leads to a marked drop of body temperature. It is known that development of hypothermia is a substantial stimulus for the adrenal-hypothalamus-hypophysis system [24-26]. Evidently, at this stage of exposure, the response of the neuroendocrine system is largely determined by change in the body's condition due to hypothermia, and it reflects the nature of its involvement in regulating defense and adaptive reactions that develop under these conditions. However, the body temperature drop leads to decrease in reactivity of the body. The dependence of change in the system under study, not only on ambient factors affecting the body, but changes in reactivity, forms an important distinction in the reaction of the hypothalamus-hypophysis-adrenal system to the combined factors. A comparison of our findings to the results of studies of reactions of this system to cooling in an ordinary gas atmosphere and to certain other extreme stimuli [6, 26, 27] shows that the response of the system in question in the second period of exposure does not develop to its potential maximum due to diminished reactivity of the organism.

In the third period (90th-120th min), there is depression of activity of all elements of the hypothalamus-hypophysis-adrenal system. This is of essential significance, since it protects it from stress, involvement in reactions related to "overregulation," and creates conditions for more efficient maintenance of vital functions during combined exposure and development of higher resistance to profound and prolonged hypothermia and acute ischemia of the brain after animals are cooled against the background of increasing hypoxia and hypercapnia.

In the recovery period (after 3 and 48 h), the functional state of the system under study continued to be altered. Evidently, this reflects two factors: extent of damage to the system in question and nature of its involvement in controlling homeostasis of the body that was impaired by exposure.

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EXCHANGE OF GASES AND PHYSICAL WORK CAPACITY IN NATIVES OF DIFFERENT GEOGRAPHIC REGIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 3, May-Jun 84 (manuscript received 8 Oct 82) pp 65-68

[Article by N. A. Agadzhanyan, A. I. Yelfimov, A. Ye. Severin and I. A. Pas (USSR and Republic of Cuba)]

[English abstract from source] A study was carried out to investigate exercise tolerance, gas exchange and external respiration of Latin-American students who lived in Moscow for a year. As controls Soviet students residing in and around Moscow were used. The above parameters were measured at a different time of day in response to a hypercapnic exposure. Exercise tolerance was determined using the test PWC_{170}. External respiration and gas exchange were investigated at rest and during 5 min exercises with a load of 1 and 2 Wt/kg body weight. CO_2 sensitivity was determined by means of the rebreathing method. In the evening the Latin-American students showed a trend towards an increase of the cardiorespiratory activity and exercise tolerance. The Soviet students did not display changes in exercise tolerance. The Latin-American students showed an increase in the morning and a decrease in the evening of external respiratory reactions. The Soviet students exhibited opposite variations. Direct alveolar measurements demonstrated an increase of pCO_2 in the alveolar air in the Latin-American students in the evening and a decrease of the parameter in the Soviet students. It is suggested that cyclic changes in external respiration in response to hypercapnia are associated with exercise tolerance.

[Text] Development of new geographic and climate zones, and the related migration of the population made it necessary to study man's adaptation to altered environmental conditions.

Investigation of adaptation to changes in organizing work and rest schedules is very important to space biology and aerospace medicine [1-3].

Previously, several authors [4-6] studied the dynamics of circadian rhythms when people moved in a meridional direction. They demonstrated changes in circadian rhythm of the subjects and its synchronization with local time within 6-10 days. However, these data were obtained with the subjects at rest.

Our objective here was to determine dependence of physical work capacity on dynamics of parameters of gas exchange and changes in external respiration reaction to hypercapnia at different times of day.

Methods

We took the gas exchange parameters as criteria of adaptive change in circadian rhythm. We compared the ventilatory reaction to hypercapnia and exercise in the morning and evening.

The study was conducted with the participation of 25 students from Central America (Cuba, Dominican Republic, Nicaragua, Panama) who were studying in Moscow for 1 year (main group) and 15 Soviet students who were residents of Moscow and Moscow Oblast (control group); in the main group, average weight was 63 kg, height 173 cm and age 23 years; in the control group, the figures were 72 kg, 178 cm and 20 years, respectively.

Examinations were made from 0900 to 1200 and 1800 to 2100 hours Moscow time. The difference between Moscow time and the local time for students in the main group was 9 h and, consequently, for them the examination times were 0000 to 0300 and 0900 to 1200 according to their local time. The test programs were identical in the morning and evening. They included the "rebreathing" test, which was performed on a Medicor universal spirograph, 30 l being the total volume of the system, for 8-10 min and two sessions on a bicycle ergometer with loads of 1 and 2 W/kg weight lasting 5 min each. The exercises were done on a Simens firm bicycle ergometer.

During these tests, we recorded the EKG in the D-S lead, gas exchange by the method of Douglas-Haldane and took samples of alveolar air. Spirography was performed before the tests.

The material was submitted to statistical processing by the Wilcoxson method for related samples.

Results and Discussion

The Table lists the dynamics of gas exchange parameters at different times of day, at rest and during physical exercise, in subjects of the main and control groups. Pulmonary ventilation ($\dot{V}_E$) at rest was somewhat higher in the evening in both main and control groups of students. During exercise loads of 1 and 2 W/kg, students in both groups showed an increase in pulmonary ventilation that was proportionate to the load. However, we found that in the main group $\dot{V}_E$ was higher in the evening than in the morning; in the control group no significant difference between morning and evening $\dot{V}_E$ levels was demonstrated.

Oxygen uptake ($\dot{V}_{O_2}$) was also higher at rest in the evening, in both the main and control groups of students. During exercise, $\dot{V}_{O_2}$ also increased with increase in load; however, we found the changes to be in different directions ($\dot{V}_{CO_2}$) in the morning and evening hours in both the main and control groups: in the main group, oxygen uptake was higher in the evening than in the morning, whereas the reverse was true for the control group. Carbon dioxide output $\dot{V}_{w_2}$

did not differ in dynamics from $\dot{V}_E$. The respiratory quotient (R) as a whole was somewhat higher in the main group, which is probably related to their diet (students from Latin American countries traditionally prefer food that is high in carbohydrates).

Dynamics of gas exchange parameters in main and control groups of students (M±m)

Parameter	Group of subjects	At rest		With following loads			
				1 W/kg		2 W/kg	
		AM	PM	AM	PM	AM	PM
$\dot{V}_E$, ℓ/min	Control	10.7 ± 0.8	12.6 ± 0.9	28.6 ± 1.5	28.8 ± 1.6	49.0 ± 2.1	48.6 ± 2.6
	Main	12.6 ± 1.4	13.2 ± 1.6	29.8 ± 1.3	30.0 ± 1.9	46.0 ± 2.8	50.8 ± 1.9
$\dot{V}_{O_2}$, mℓ/min	Control	388 ± 32	394 ± 26	1336 ± 118	1208 ± 72	2197 ± 107	2167 ± 102
	Main	322 ± 21	344 ± 21	1150 ± 50	1225 ± 83	1807 ± 114	1935 ± 85
$\dot{V}_{O_2}$/W mℓ/min/W	Control	5.43 ± 0.44	5.61 ± 0.63	18.70 ± 1.65	16.81 ± 0.84	15.28 ± 0.62	15.06 ± 0.52
	Main	5.05 ± 0.29	5.27 ± 0.38	17.68 ± 0.76	18.65 ± 0.89	13.78 ± 0.64	14.82 ± 0.46
$\dot{V}_{CO_2}$, mℓ/min	Control	307 ± 17	371 ± 29	1068 ± 53	1053 ± 68	1989 ± 97	2051 ± 101
	Main	336 ± 33	345 ± 23	1067 ± 66	1099 ± 62	1854 ± 116	2042 ± 84
R, units	Control	0.81 ± 0.01	0.93 ± 0.07	0.82 ± 0.04	0.89 ± 0.04	0.91 ± 0.03	0.95 ± 0.03
	Main	1.03 ± 0.05	1.01 ± 0.05	0.93 ± 0.04	0.91 ± 0.02	1.02 ± 0.03	1.06 ± 0.03
CUO_2, mℓ O_2/ℓ	Control	45.4 ± 4.6	38.7 ± 3.5	56.4 ± 2.3	51.2 ± 1.7	55.7 ± 2.8	54.8 ± 2.3
	Main	35.1 ± 2.9	34.2 ± 2.2	48.3 ± 1.5	49.6 ± 1.7	48.6 ± 1.6	46.8 ± 1.5
O_2 pulse, mℓ O_2/beat	Control	4.81 ± 0.55	5.52 ± 0.97	12.90 ± 1.73	11.16 ± 0.76	15.66 ± 0.55	15.40 ± 0.67
	Main	4.17 ± 0.34	4.22 ± 0.22	11.1 ± 0.71	11.20 ± 0.97	12.35 ± 0.82	13.16 ± 0.75

Key: CUO2) coefficient of oxygen utilization

Oxygen uptake changes the most demonstratively of all gas exchange parameters, both in relation to load and body weight. Analysis of $\dot{V}_{O_2}$/W showed that it decreased with increase in load. As compared to findings obtained at different times of day in the control group, we observed higher values for this parameter in the morning, whereas in the main group this was referable to the evening.

It is generally considered that a decrease in uptake of O_2/V load is indicative of economy of energy expenditures and, as a whole, reflects conditioning [7-9]. However, in this case, it was apparently related to other processes.

This is reinforced also by the data on acid-base state of blood. Thus, it was found that there was a higher concentration of acid metabolic products in blood of the control group of students in the evening after exercise of 2 W/kg (base excess--BE--constituted 2.26 meq/ℓ), remaining at a low level in the morning (BE = 0.80 meq/ℓ). In the main group of students, the changes in acid-base state were the opposite: base excess constituted 3.13 meq/ℓ in the morning after an exercise load of 2 W/kg and 2.06 meq/ℓ in the evening.

Thus, the decrease in oxygen uptake per unit load in the evening for the control group and morning for students in the main group is indicative of more active involvement of anaerobic glycolytic processes in energy production.

Perhaps, respiratory sensitivity to CO_2 plays a significant part in this process [10, 11]. Thus, in the 8th min of rebreathing pulmonary ventilation in the control group constituted 0.66 ℓ/mm Hg CO_2 in the morning and 0.77 ℓ/mm Hg CO_2 in the evening; the figures for the main group of subjects were 0.75 and 0.69 ℓ/mm Hg CO_2, respectively. Partial CO_2 tension in inhaled air in the 8th min of rebreathing was identical in control and main groups of students, constituting 44-46 mm Hg.

On the basis of the above values of ventilatory reaction, we can conclude that the control group of students are more sensitive to CO_2 in the evening and the main group, in the morning. This conclusion is also confirmed by data on maximum breathing capacity (MBC), obtained by spirography. Thus, in the control group MBC constituted 143 ℓ/min in the morning and 139 ℓ/min in the evening, whereas for the main group of students the figures were 102 and 104 ℓ/min, respectively. Partial carbon dioxide tension in alveolar air and blood is probably lower with higher sensitivity to CO_2 and, consequently, total CO_2 content of the body is smaller. During voluntary hyperventilation in this case, there is faster onset of hypocapnia and apnea. The reverse process apparently occurs with decreased sensitivity to CO_2. Our findings conform well with the data in [12], where development of hypocapnia and increase in acid metabolic products was demonstrated at 1800 hours in the control group of subjects.

Direct measurement of partial CO_2 tension in alveolar air confirmed the results obtained with rebreathing. Thus, resting partial CO_2 pressure in alveolar air was 41 mm Hg in the morning and 39 mm Hg in the evening in the control group of students, and in the main group the figures were 33.6 and 34.7 mm Hg, respectively.

Interestingly, oxygen pulse also echoed the changes in gas exchange parameters. At rest, the main and control groups of students showed a higher oxygen pulse in the evening than in the morning. During exercise, this parameter declined in the evening in the control group of students; the reverse was found in the main group of subjects.

Significant findings were made with regard to one of the principal indicators of physical work capacity, PWC_{170}. As was the case when we analyzed gas exchange parameters, the main group of students showed an increase in PWC_{170} from 165.5±15.0 W in the morning to 181.6±12.3 W in the evening. The demonstrated difference was statistically significant (Wilcoxson's criterion for related pairs $T_2<T_{0.05}$). In Soviet students PWC_{170} showed virtually no change, constituting 197.3±11.5 W in the morning and 202±15.4 W in the evening.

Thus, the data obtained concerning exchange of gases and physical work capacity are indicative of changes in different directions in gas exchange as a whole during exercise in the main and control groups at different times of day. In addition, the data obtained at rest for both groups of students changed in the same direction in the course of the day.

Perhaps such differences occurred because of differences in schedule for the day and mealtime in the main and control groups. For example, the control group of students performed tasks more willingly in the morning and subjectively rated the test loads as lighter, as compared to evenings. Moreover, the control group usually had a more substantial breakfast, which constituted 25-30% of the daily food intake in most cases. Conversely, the main groups of students had a "token" breakfast and, in a number of instances, they preferred to skip breakfast. As a rule, the main group consumed an abundant supper, at least 25-30% of the daily food intake. The daily schedule was also interesting: it was rare for any of the main group students to go to sleep before 2400 and get up before 0800. In more than half the cases, the control group of students fell

asleep at 2300 hours and w ke up at 0700 hours. Probably this schedule was one of the reasons for the observed dynamics of gas exchange parameters.

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RAT BEHAVIOR IN SELECTION OF NEGATIVE STIMULUS: PAIN OR EXPOSURE TO ELECTROMAGNETIC FIELD

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 3, May-Jun 84 (manuscript received 3 Mar 83) pp 68-71

[Article by B. I. Davydov, I. B. Ushakov, V. S. Tikhonchuk and A. A. Galkin]

[English abstract from source] A new experimental model of two conflicting motives has been developed and tested on rats. The motives are to escape painful stimulation and subsequent microwave irradiation at a dose rate of 500 mWt/cm^2 under normal conditions and disturbed thermal regulation due to gamma irradiation of the head. It is found that microwave effects cannot be entirely attributed to the body temperature gradient.

[Text] Investigation of animal behavior as related to exposure to ionizing and nonionizing radiation under complicated conditions of two or even three motivations is of definite interest, not only to electromagnetobiology, but to radiation psychophysiology. Under complicated conditions of multiple motivations, the organism is in an extremely "confused" state and compelled to choose one of the negative stimuli on the principle of taking the minimal risk. Evaluation of probability of forthcoming events and choice of tactics in reacting to this probability hold a key position in organization of behavior [1].

There are several works dealing with investigation of behavioral reactions of different animal species exposed to electromagnetic (nonionizing) radiation [2-6], as well as similar studies in the area of radiobiology of ionizing radiation [7]. It was interesting to investigate these two factors simultaneously, using them as reciprocal test factors, according to criteria of capacity to function.

We investigated a new model of a "clash" between two motivations: pain-causing stimulation and exposure to an electromagnetic field (EMF) at radio frequencies. Our objective was to determine the extreme factor that is the most significant at a concrete time. In essence, the experiments confirming the principle of taking the least risk consisted of the following.

We developed in rats a stable reflex for avoidance of an electric shock. The rats would jump on a smooth, freely revolving rod or on a narrow shelf (Figure 1). The method was always used in only one of these versions. We considered as the criterion of training 100% performance of a task by a group

of 10 animals. This was usually achieved after 12-13 tests. There were 20-min intervals between tests. The animals on the rod, in a relatively unsupported position, were required to demonstrate some coordination to stabilize their body in relation to the center of gravity and some muscular exertion. The minimum time that an animal could hold on to the rod was 30 min. The rats could spend a long time on the shelf, but in our experiments it was limited to 30 min. One day after development of a stable pain avoidance reflex, animals on the rod or shelf were exposed to 2.4 GHz microwaves, and irradiation conditions were close to $\bar{E}$ polarization on the rod and $\bar{N}$ polarization on the shelf. Exposure at a dose rate of 500 mW/cm^2 continued until the animal avoided this stimulus; it was discontinued after the animal jumped down on the electric floor. Thus, irradiation time corresponded to the time spent by rats away form the painful electric shock stimulus. We conducted two series of tests, with 5-fold irradiation in each at intervals of 20 min. All of the tests lasted 90 min. We took the animals' rectal temperature before and after exposure to microwaves. Mean base rectal temperature constituted 38.0±0.3°C.

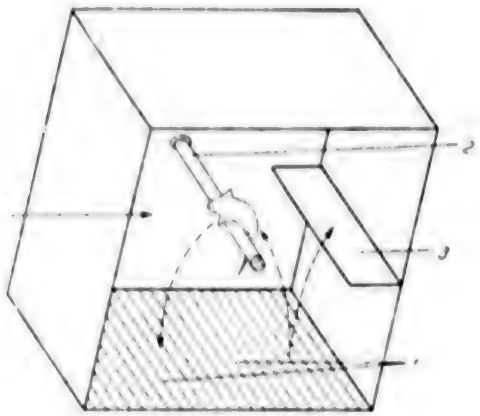

Figure 1.
General view of set-up in study of behavioral double-avoidance reaction. Dash-lined arrow shows direction of avoidance of rats on rod and shelf; solid-lined arrow shows direction of EMF irradiation
1) electric floor
2) freely revolving smooth rod
3) shelf

Analysis of the data illustrated in Figure 2a clearly shows a correlation between time spent in EMF and rise of rectal temperature. We were impressed by the fact that, during the complex motor reaction of holding on to a revolving rod, the animal spent more time in the EMF than when it was on the shelf, when no adequate muscular tension was required of the rat. It can be assumed that this is related to the motivation of holding on to the revolving rod, with significant activation of visual and vestibular analyzers. The fact that, in the version with the shelf, the rectal temperature increment during irradiation was not only not lower, but even somewhat higher on the average is somewhat paradoxical (Figure 2a).

In these studies, the EMF energy density was rather high for rats, so that exposure to microwaves turned out to be a stronger motivation than the pain of electric shock: the time the rats spent on the rod was reduced to less than 1/60th, and the reduction was even greater in the version with the shelf.

The two variants of experimental conditions (rod and shelf) demonstrated differences in the animals' reaction to the EMF, while the decrease in correlation (with a tendency toward the reverse relationship) between $\Delta T°$ and t (compare the mean value of t in the version with the shelf, where it was 21°C at $\Delta T°$ = 1.8°C, to its value in the version with the rod, where t = 32°C and $\Delta T°$ = 1.4°C) indicates that the effect of EMF avoidance is related not only to elevation of animals' body temperature.

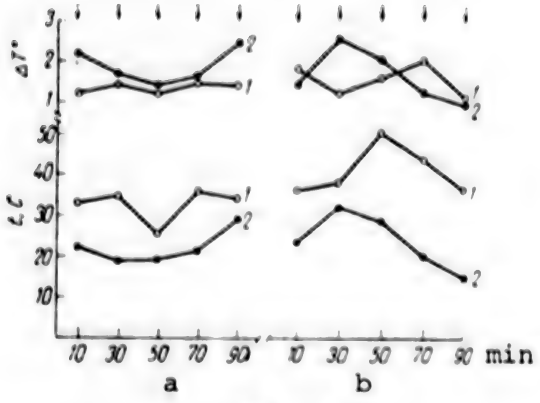

Figure 2.
Reaction to EMF (2.4 GHz) of rats with previously developed stable conditioned reflex pain avoidance reaction

a) without ionizing radiation
b) after exposure to radiation in a dosage of 5.16 C/kg (20 kR) delivered to head
1) version with avoidance of electricity by jumping on rod
2) same, with jumping on shelf
t) time (s) spent on rod or shelf corresponding to time in EMF
$\Delta T°$) rectal temperature (C°) increment during exposure to electromagnetic radiation

Arrowheads show number of exposures to microwave field at dose rate of 500 mW/cm^2.

X-axis, duration of entire experiment with electromagnetic testing of animals. In Figure 2a, starting point is time of placement of rats for testing in experimental chamber; Figure 2b shows end of exposure of head to ionizing radiation. Ten rats were tested in each variant of the method.

Subsequent studies amounted to a search for means of disrupting heat regulation, as well as body functions involved in the animal's coordination. In this case, we could have expected faster avoidance of the microwave field in the version with the rod. We tried to create such a stimulus using high doses of γ-radiation. This variant with a combination of two factors could also serve for the opposite problem: to evaluate the state of the irradiated organism by means of an EMF load in the microwave range. An analogous approach was used in relation to total-body exposure of animals to ionizing radiation in doses targeted for the hemopoietic system [8, 9].

High doses of γ-radiation should lead to impairment of heat regulation [10-12] and other functions and, consequently, distort the animal's behavioral reaction to EMF. It could also have been assumed a priori that high doses of ionizing radiation would elicit not only impairment of heat regulation, but body temperature drop and, consequently, lead to increase in reaction time to the microwave field.

The rats' head was exposed to ^{60}Co γ-rays in a dosage of 5.16 C/kg (20 kR) at a dose rate of 1.7 mA/kg. With this dosage, the first neurological symptoms (tremor, ataxia) appeared in the rats 60-90 min after irradiation. Rectal temperature taken 10 min after exposure to γ-radiation dropped by an average of 1°C.

Animals exposed to ionizing radiation reacted with diminished sensitivity to EMF, particularly in the 1st postirradiation hour: in both versions, the same animals spent more time in the EMF (Figure 2b) than they did on the preceding experimental day (see Figure 2a).

There was no impairment of animals' coordination up to virtually the 60th min after exposure to γ-radiation (58±16 and 78±21 min in the variants with the shelf and rod, respectively), i.e., there had not been time for neurological manifestations to develop. This was manifested by the rats' equal ability to jump up either on the shelf or rod. However, total impairment of capacity to function occurred

later than the rats showed the first clinical symptoms of the cerebral form of radiation sickness. The temperature increment was virtually the same as before γ-irradiation, within 1-2°C, and it was correlated with duration of exposure to microwaves. It should be noted that, in all cases, absolute value of rectal temperature did not exceed 40°C. Preliminary experiments also confirmed that the reaction to EMF cannot be attributed entirely to the gradient of rectal temperature increase. Apparently, local specific dose rates, particularly in the region of the head, play a large part.

In conclusion, it must be mentioned that, in the future, this method will apparently permit determination of the dose rate, by lowering the force of microwave exposure, that will be comparable in strength of motivation to the strength of the reflex to a painful stimulus. In addition, this model can be used for the study of the combined effect of extreme environmental factors on behavioral reactions of animals.

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EFFECT OF STATIONARY MAGNETIC FIELD ON BIOELECTRIC ACTIVITY OF RABBIT BRAIN EPILEPTOGENIC FOCI

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 3, May-Jun 84 (manuscript received 22 Nov 82) pp 71-75

[Article by L. I. Tyvin]

[English abstract from source] The effect of a constant magnetic field (CMF) on the hypersynchronic activity foci produced by penicillin microinjections to the rabbit hippocampus or sensorimotor cortex was investigated. The control animals showed a higher epileptiform activity in the left than in the right hemisphere. The CMF exposure enhanced the difference between the hemispheres, increased drastically the number of epileptiform discharges between attacks and the number of electrographic correlates of attacks in hippocampal foci. The epileptiform activity of cortical foci was practically independent of the CMF exposure. It is assumed that the CMF influences oxidative processes in neurocytes and facilitates their epileptization. This also induces a hyperactivity focus in the hippocampus whose threshold of convulsive attacks is the lowest among the central nervous system structures, the cortex including.

[Text] A study was made of effects of stationary magnetic field (SMF) on epileptogenic foci (EF) in the hippocampus or sensorimotor cortex of the rabbit, which were generated by microinjections of penicillin. These structures were chosen because of their high sensitivity to SMF [1] and large part they play in the pathogenesis of epilepsy [2]. Let us mention that simulation of hypersynchronous activity of neuronal ensembles of the brain makes it possible to gain deeper understanding of physiological processes taking place in its different parts which are aimed at maintaining normal excitability of cellular elements and structures [3].

Methods

Experiments were conducted on 29 chinchilla rabbits of both sexes, which were divided into four groups. In control animals of the 1st and 3d groups (10 rabbits in each), EF were produced in the hippocampus (1st group) or sensorimotor cortex (3d group), without submitting them to any other factors. Experimental rabbits of the 2d (4 animals) and 4th (5 animals) groups were exposed to SMF.

Chemical electrodes were implanted in stereotactic coordinates [4] in the 1st and 2d groups of animals, in the left and right dorsal hippocampus, and bipolar electrodes were placed in the region of the sensorimotor cortex. The 3d and 4th groups of rabbits had chemical electrodes implanted in the left and right sensorimotor cortex, while bipolar electrodes were placed in the left and right dorsal hippocampus. Bipolar electrodes were implanted to make sure, before starting the experiment, that there was no pathology on electroencephalograms (EEG) of different parts of the brain, as well as to observe irradiation of hypersynchronous activity from the epileptoid structure to intact parts of the central nervous system. In each experiment, EF were formed by injecting with a microsyringe, through the cannual of the chemical electrode, a solution of penicillin (100 IU in 0.001 mℓ double distilled water into the hippocampus, or 150 IU in 0.002 mℓ into the cortex) in one of the following structures: left or right hippocampus, left or right cortex.

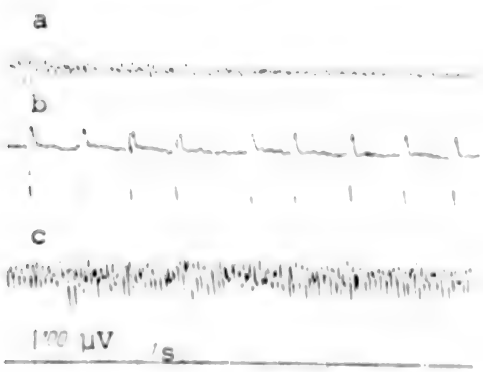

Figure 1.
EEG of rabbit hippocampus before and after penicillin injection
a) before injection
b) epileptiform discharges between seizures
c) segment of electrographic correlate of seizure

EF were produced 6 times in all of the rabbits, alternately in the right and left hippocampus (or right and left cortex), at 3-day intervals. Bioelectric potentials of the brain were recorded continuously for 5 min before (Figure 1a) and 120 min after producing the focus of hypersynchronous activity. Several minutes after injecting the antibiotic into the brain, high-amplitude (up to 500 μV) one- or two-phase impulses appeared on the EEG at a rate of 10-70/min--interseizure epileptiform discharges (Figure 1b) which lasted about 200 ms. In the course of the experiment, the EEG also showed electrographic correlates of seizures (ECS; Figure 1c)--a series of discharges with amplitude of 300-600 μV and frequency above 10 Hz, recurring 6-12 times in the course of the 2-h experiment. We counted the total number of ECS per 10-min interval, as well as mean number of interseizure epileptiform discharges (spikes; IED) per minute of EEG tracing. The counts were made in the lead from the structure where the focus was produced and in the lead from the symmetrical structure in the contralateral hemisphere, where a mirror focus appeared.

In control animals, all six tests involving producing of EF were performed without use of SMF. Experimental animals first received penicillin in the left hemisphere and then in the right, under the same conditions as for control animals. The rabbits head was placed in an SMF 60 min before the 2d and 3d epilepsy-inducing injections, exposing each of the contralateral brain structures, and exposure was continued to the end of the experiment. Thus, all of the animals, with the exception of those in the control group, were exposed 4 times to the field, each exposure session lasting 180 min. A horizontal magnetic field, with induction of 60 mT, which was homogeneous in the region of the hippocampus and sensorimotor cortex, was generated with a permanent magnet, with 60×65 mm pole tips and 75 mm distance between them.

Similar characteristics of epileptiform activity (for example, number of spikes recorded between the 10th and 20th min of the experiment with the third production of epileptic focus in left hippocampus) were averaged for the number of animals per group. Results obtained with the first EF-producing injection were taken as the base (100%) and the corresponding parameters of hypersynchronous activity after the second and third penicillin injection into a given structure were related to it. For a definitive description of various types of epileptiform activity, we used series of 12 values that corresponded to the mean relative levels of interseizure or paroxysmal activity in each of the 10-min intervals of the experiment. In addition, we estimated the mean value of parameters of EF activity for the entire experiment.

The Nairi-2 computer was used for statistical processing of information, comparing analogous series for control and experimental groups of rabbits, with use of the U nonparametric criterion of Wilcoxson-Mann-Whitney.

Results and Discussion

Effect of SMF on Activity of Epileptogenic Focus in Hippocampi

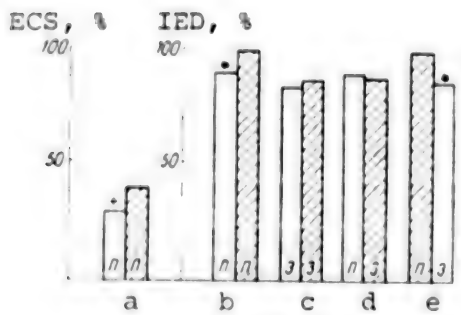

Figure 2.
Comparative activity of primary (п) and mirror (з) epileptogenic foci produced in the right (white bars) or left (crosshatched bars) hippocampus of control rabbits (1st group)
a) number of ECS in primary foci of right and left hippocampus
b) number of IED in primary foci of right and left hippocampus
c) number of IED in mirror foci of right and left hippocampus
d) number of IED in primary foci of right hippocampus and corresponding mirror foci of left hippocampus
e) number of IED in primary foci of left hippocampus and corresponding mirror foci of right hippocampus

Experiments with the 1st group of control animals, with EF in the hippocampus, revealed a reliable increase in number of ECS in primary foci of the left hippocampus, as compared to primary foci in the right one (Figure 2a). Interseizure activity of the primary focus in the left hippocampus was also reliably higher than in the primary focus of the right hippocampus (Figure 2b). The correlation between spike activity of primary and mirror foci in the same rabbits is illustrated in Figure 2c,d,e. The results are indicative of greater predisposition for epileptization in limbic structures of the left cerebral hemisphere of rabbits, as compared to the right.

In the 2d group of rabbits, the predominance of the left hippocampus over the right, with regard to number of ECS noted in the control, increased appreciably under the influence of SMF (Figure 3a). The data illustrated in Figure 3b,c also indicate that the number of ECS of primary foci in

← Y-axis, number of IED or ECS with second and third EF-producing injections (% in relation to first injection in given hippocampus). Here and in Figure 3, asterisk shows $P<0.05$ and "+" sign shows $P<0.01$

the left and right hippocampus of experimental rabbits increased appreciably, as compared to the same parameters for the first group of animals.

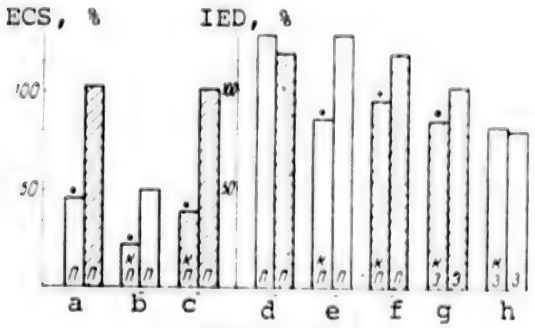

Figure 3.
Comparative number of ECS (a-c) and IED (d-h) in primary (П) and mirror (З) epileptogenic foci produced in left or right hippocampus of control rabbits (K--1st group) and with exposure of head to magnetic field (2d group)
Here and in Figure 4: the dots indicate $P<0.001$

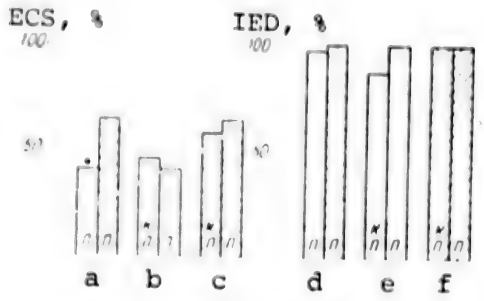

Figure 4.
Comparative number of ECS (a-c) and IED (d-f) in primary epileptogenic foci produced in left or right cortex of control rabbits (K) (3d group) and with exposure of head to SMF (4th group)

The number of IED in the left and right hippocampus (primary focus) was virtually the same (Figure 3d), but when compared with the control we found that interseizure activity increased significantly both in the left and right hippocampus of experimental rabbits (Figure 3e,f). Such intensification of pathological activity occurred in the left hippocampus, but not in the right, in the mirror focus (Figure 3g,h).

Thus, SMF increased the number of ECS and intensified interseizure epileptiform activity in foci of heightened neuronal excitability produced in the rabbit hippocampus. It was also instrumental in increasing interhemisphere differences between reactions of left and right hippocampus to the agent (in this case, penicillin) that epileptisized neurons of this structure.

Effect of SMF on Activity of Epileptogenic Focus in Region of Sensorimotor Cortex

Production of EF in the left or right sensorimotor cortex of control rabbits (3d group) failed to demonstrate reliable differences between number of ECS and IED in foci of the left and right cortex; however, there was still a tendency toward greater values of these parameters in the EF of the left cortex than the right.

After exposure to SMF, experimental rabbits (4th group) failed to demonstrate reliable changes in activity of the EF in the left and right cortex, as compared to the 3d control group of animals (Figure 4). It should be noted, however, that the interhemisphere difference in number of ECS generated by EF in the left and right cortex became reliable (see Figure 4), unlike the animals in the 3d control group. Since there was virtually no difference in epileptiform activity of primary and mirror foci in the 3d and 4th groups of animals, we have submitted data only for the primary focus.

It is known that the central nervous system responds to SMF with processes that facilitate onset and distribution of excitation in neuronal ensembles [5], increased synchronization of the EEG and even appearance of epileptiform discharges on it [6].

The existing information about mechanisms of effect of SMF on biological systems enable us to expound some hypotheses on how the SMF can cause intensification of EF activity. It is known that exposure to SMF elicits serious changes in cell morphology [7]. Numerous reactive changes have also been noted in the ultrastructure of neurons and glial cells, as well as in synaptic endings [8]. Such changes could lead to compression of neurons, changes in their metabolism, decline of excitation threshold and, as a result, their epileptization.

It was demonstrated [9, 7] that SMF and mild hypoxia elicit similar changes in the body: tissue oxygen tension drops, oxygen-binding properties of hemoglobin worsen and there is decrease in conversion half-life. Significantly, animal adaptation to SMF improves their tolerance of hypoxia and vice versa [10].

Perhaps the disturbances in oxygen metabolism caused by SMF, like hypoxia which is one of the etiological factors of epilepsy [2], facilitate involvement of many neurons in the epileptic process and formation of chains over which the convulsive discharges circulate.

Potassium and sodium concentrations in the brain diminish under the influence of SMF [11]. There is drastic activation of lipid peroxidation reaction in hyperactive foci [12]. A similar change in tissular metabolic processes occurs when tissues are placed in an SMF [13], and the possibility cannot be ruled out that lipid peroxidation could be activated in the presence of hypoxia [14].

The described metabolic changes can elicit depolarization changes and lead neurons to a state of epileptic readiness.

The experimental results indicate that EF produced in the left hippocampus are more active than those produced in the right hippocampus, and this difference increases under the influence of SMF. An analogous effect, but considerably milder, occurred in the sensorimotor cortex. Intensification of interhemisphere differences under the effect of SMF is perhaps related to the fact that the characteristics of SMF of the left and right hemispheres may differ in direction and values [15].

In this study, we failed to demonstrate a clearcut provocative effect of the tested field on EF in the sensorimotor cortex. At first glance, this finding is inconsistent with the known data concerning the high sensitivity of the cortex to SMF [1]. However, it should be borne in mind that any functional EF is instrumental in mobilizing inhibitory mechanisms aimed at eradicating it [16]. The inhibitory mechanisms of the sensorimotor cortex of the brain are more refined than those of the hippocampus, as indicated, in particular, by the fact that EF are produced much more easily in the hippocampus [17, 18]. For this reason, it can be assumed that, when simulating cortical epilepsy, mobilization of stronger inhibitory systems of the neocortex, as compared to the hippocampus, prevents the provocative effect of SMF on foci of neuronal excitation in this structure.

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EFFECT OF HIGH AMMONIA CONTENT IN PRESSURE CHAMBER ATMOSPHERE ON HUMAN ADRENOCORTICAL SYSTEM FUNCTION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 3, May-Jun 84 (manuscript received 28 Mar 83) pp 75-77

[Article by S. Kalandarov, V. P. Bychkov, I. D. Frenkel' and T. I. Kuznetsova]

[English abstract from source] The effect of various ammonia concentrations in an enclosed atmosphere on man's adrenocortical system was investigated in five experiments on 20 young healthy test subjects. The most pronounced changes in the adrenocortical system developed when the ammonia content was 5 mg/m^3.

[Text] Toxic trace substances, including ammonia, may accumulate in the atmosphere of pressurized compartments as a result of man's vital functions and use of polymers [1]. For this reason, it is of practical and theoretical interest to investigate the functional state of the adrenosympathetic system (ASS) and adrenal cortex during long-term exposure to low concentrations of ammonia.

In the literature, there are mainly the results of physiological studies of low concentrations of ammonia. According to the data of a number of authors, exposure to an atmopshere with up to 2-5 mg/m^3 ammonia for 7-8 h elicited a decrease in bioelectric activity of the brain and redox processes in man [2-5]. The effect of ammonia on ASS and adrenocortical function was not investigated.

We submit here the results of a study of the functional state of the ASS and adrenal cortex during long-term exposure of man to different concentrations of ammonia in a pressure chamber.

Methods

The studies were conducted in a 24 m^3 pressure chamber at normal barometric pressure. A total of 20 subjects (4 in each) participated in 5 studies.

In the first and second studies, the ammonia concentration in the pressure chamber was held at 2.1±0.1 to 5.1±0.1 mg/m^3. Duration of exposure constituted 37 and 17 days, respectively. In the third study, ammonia concentration was kept at 2.1±0.1 mg/m^3 for 35 days, with brief (for 1 day) rise to 9.8±0.1 mg/m^3.

In the 4th and 5th studies, each of which lasted 20 days, exposure to ammonia in concentrations of 2.1±0.1 and 5.1±0.1 mg/m^3 was combined with elevation of temperature (26-28°C) and increase in humidity (70-80%). The set concentration of ammonia in the pressure chamber was monitored strictly. The O_2 level in the chamber atmosphere was held at 21±2%, and CO_2 did not exceed 0.4-0.6%. The meals of the subjects consisted of a specially developed diet, which was balanced in its main nutrients, totaling about 3000 kcal.

We assessed ASS functional state according to catecholamine (CA) excretion, as assayed by the fluorimetric method [6]. To evaluate adrenocortical function, we assayed 17-hydroxycorticosteroids (17-HCS) in 24-h urine by the method of Reddy and Brown [7, 8] and 11-hydroxycortisteroids (11-HCS) in blood plasma (total, protein bound and free fractions). We used the method of deMoor et al. [9] as modified by L. V. Pavlikhina et al. [10] for separate determination of protein-bound and free forms of 11-HCS. Quantitative assays of total 11-HCS and their fractions were made by the fluorimetric method of deMoor et al. [11] as modified by Yu. A. Pankov and I. Ya. Usvatova [12].

Results and Discussion

The changes in Ca and corticosteroid levels were in the same direction in all the studies. Tables 1 and 2 list averaged values for these parameters for the entire period of our studies.

Table 1. Changes in CA (in μg) and 17-HCS (in mg) content of 24-h urine (M±m)

Parameter	Norm	Ammonia concentration in pressure chamber				
		with optimum microclimate parameters			with poorer microclimate	
		2.1±0.1	5.1±0.1	9.8±0.1	2.1±0.1	5.1±0.1
Epinephrine	4.4±0.30	5.5±0.27	7.6±0.68	5.3±0.65	4.0±0.5	5.3±0.2
Norepinephrine	15.4±1.08	18.1±1.35	14.2±1.46	19.9±2.88	12.2±1.3	12.1±3.2
DOPA	23.9±1.57	24.1±1.38	24.2±0.89	17.1±2.04	20.6±2.14	23.0±2.64
Dopamine	205.9±11.19	216.2±18.44	187.9±9.23	174±14.4	139.5±3.84	203.1±12.5
17-HCS	5.6±0.34	8.1±0.16	11.3±2.63	12.7±0.92	7.4±1.17	9.9±2.03

Table 2. Changes in levels of total, protein-bound and free fractions of 11-HCS in blood plasma (M±m)

11-HCS fraction	Norm	Ammonia concentration in pressure chamber				
		optimum microclimate			Poorer microclimate	
		2.1±0.1	5.1±0.1	9.8±0.1	2.1±0.1	5.1±0.1
Total	21.0±1.27	25.8±1.04	22.9±1.26	33.3±1.4	26.4±0.9	25.5±2.63
Protein-bound	18.1±1.15	21.5±0.58	18.4±1.29	23.7±0.61	22.0±0.84	20.5±2.50
Free	2.9±0.06	4.3±0.87	4.5±0.6	9.6±0.79	4.4±1.5	5.0±0.57

There was considerable increase in epinephrine (E) content of urine when ammonia level in the pressure chamber was 2.1±0.1 mg/m^3 (P<0.02). Norepinephrine (NE) excretion, as well as that of biological precursors of E and NE--DOPA and dopamine--changed insignificantly (see Table 1). There were also some changes in adrenocortical function, as indicated by the increased 17-HCS concentration in 24-h urine (P<0.001) and in total 11-HCS content of plasma (P<0.01).

A drastic elevation of E level (P<0.001) in 24-h urine was demonstrated with ammonia concentration of 5.1±0.1 mg/m^3 in the pressure chamber, whereas NE decreased somewhat, while DOPA and dopamine levels fluctuated over close to a normal range. At the same time, there was significant increase in concentration of 17-HCS (P<0.05) and free 11-HCS fraction (P<0.01) (see Table 2).

When ammonia concentration was increased to 9.8±0.1 mg/m^3 (for 1 day), against the background of continuous exposure to a concentration of 2.1±0.1 mg/m^3 for 35 days, the E and NE levels differed little from normal values. However, under these conditions, there was reliable decrease in DOPA (P<0.02) and significant increase in 17-HCS concentration in 24-h urine (P<0.001) and free 11-HCS fraction in blood plasma (P<0.001).

We failed to demonstrate appreciable changes in ASS function under the combined effect of ammonia (2.1±0.1 mg/m^3) and higher temperature (26-28°C) and humidity (70-80%). There was only a brief decrease in dopamine of 24-h urine (P<0.001) and increase in concentration of total 11-HCS in blood plasma (P<0.002).

We observed elevation of E level (P<0.05), 17-HCS (P<0.05) and free 11-HCS fraction in blood plasma (P<0.002) with increase in concentration of ammonia to 5.1±0.1 mg/m^3 against the background of increased temperature and humidity.

The results of our studies revealed that the most marked changes in parameters characterizing ASS and adrenocortical function were observed with an ammonia concentration of 5 mg/m^3 in the pressure chamber, which is indicative of the subjects' marked reaction to these conditions.

Our data should be taken into consideration when setting the duration of man's exposure to an atmosphere containing different concentrations of ammonia.

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EFFECT OF LIVING CONDITIONS IN CONFINED SPACE ON FORMATION OF BACTERIAL AEROSOL

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 3, May-Jun 84 (manuscript received 26 Apr 83) pp 77-80

[Article by G. O. Pozharskiy]

[English abstract from source] The effect of environmental conditions (the presence of a different number of people, various parameters of the atmosphere, operation of life support systems) on the formation of bacterial aerosol has been investigated. If the number of people in the enclosure increases, the bacterial aerosol formation depends primarily on the system of atmosphere conditioning. If the system functions, the occurrence of microorganisms on the internal surface grows. These findings may be used to design life support systems and to develop special measures that provide hygienic and antiepidemic conditions in a manned enclosure.

[Text] It is important and necessary to investigate the mechanism of transmission of microorganisms from one individual to another during long-term spaceflights, due to the changes in automicroflora of cosmonauts and requirements of providing for epidemic-free performance of crews [1-4]. The mechanisms of exchange of microorganisms between people in manned pressurized rooms, including spacecraft cabins, depends on the concentration and structure of bacterial aerosol formed under these conditions [5]. Information is furnished in the literature about involvement of different life-support systems, in particular the air-conditioning systems, in the process of spread of microorganisms [6-7].

Our objective here was to investigate the intensity of accumulation of microorganisms in the atmosphere of an inhabited pressurized compartment as related to number of people and operation of air-conditioning equipment.

Methods

The distinctions of formation of bacterial aerosol were studied under laboratory conditions, as well as in the course of 6 studies in confined rooms with the participation of 14 subjects. The Table lists the characteristics of the principal conditions of these studies. Samples of atmospheric microflora in the pressure chamber were taken by the aspiration and sedimentation method using Krotov apparatus [8].

Characteristics of principal experimental conditions

Space used and its size	Performance of life-support systems	Test No	Duration of test, days	Number of people	Microclimate	
					temp., °C	relative humidity, %
Pressure chamber, 26 m^3	Air conditioners not working	1 2 3	7 4 2	1 2 4	Gradual increase to 32	90
Pressure chamber, 26 m^3	Air-conditioners working	4 5 6	7 4 2	1 2 4	17±1	45—50
Enclosed room, 8 m^3	Fan not working	7	0.04	1	20±2	40—60
	Fan working	8	0.04	1		

Samples of microflora were collected from the inside surfaces of the pressure chamber 4 times a day using the washing off method that is customary in sanitation bacteriology.

In all of the experiments, we used 5% blood agar. The cultures were placed in an incubator and kept at a temperature of 37°C for 2 days, after which we counted the colonies of microorganisms.

Results and Discussion

As can be seen from the data illustrated in Figure 1a, b, the concentration of bacterial aerosol in the pressure chamber depended on the number of people in it. It was shown that, on the 1st day of the study, when the air-conditioning system was not working (see Figure 1a, b; solid line 1), the presence of 1 person corresponded to a concentration of bacterial aerosol of 300 microorganisms/m^3 (mic/m^3); with 2 people it increases to 3000 mic/m^3, with 4 to 30,000 mic/m^3, i.e., 2- and 4-fold increases in size of crew were associated with 10- and 100-fold increases in concentration of bacterial aerosol. As shown in the same figure, when the air-conditioning system was operating (dash line), bacterial aerosol concentration decreased to 1/4th-1/10th with 2-4-fold increase in number of people in the chamber. This is indicative of the predominant influence of the air-conditioning system on the process of formation of bacterial aerosol in manned pressurized rooms. Presence of 1 person in the enclosed room and operating air-conditioning systems constituted the conditions that made it possible to maintain the lowest concentration of bacterial aerosol (200-300 mic/m^3) (see Figure 1, dash line 1). With the air-conditioning systems working and increase in number of people in the compartment by 2 and 4 times, the concentration of bacterial aerosol increased by 4 and 10 times, which corresponded to 800 and 10,000 mic/m^3 on the 2d day of the studies (see Figure 1, dash lines 2 and 3). Consequently, the capability of the air-conditioning system to maintain an optimum concentration of bacterial aerosol could be limited by the presence of a specific number of people (in our case, 1 person) in the pressurized room. With increase in number of people under these conditions, there may be a drastic increase in concentration of bacterial aerosol.

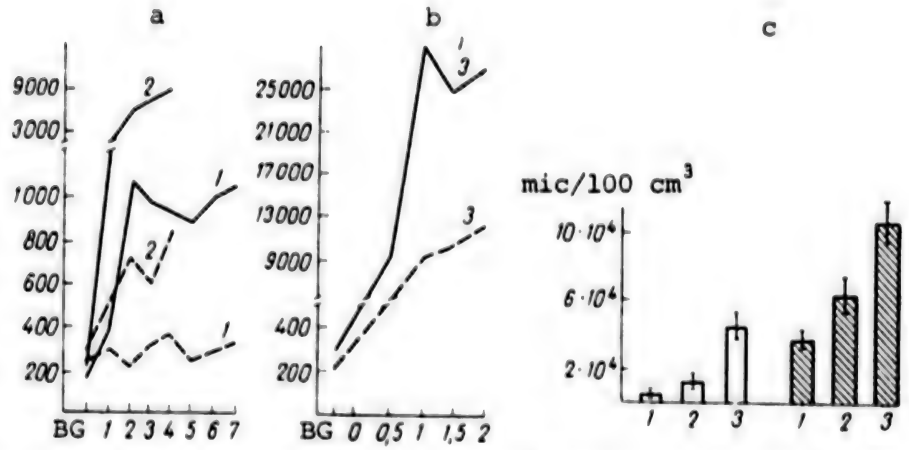

Figure 1. Dynamics of concentration of bacterial aerosol in pressurized room with 1, 2 (a) and 4 (b) people, and dynamics of number of microorganisms/100 cm^3 inside surface of the room (c)

a, b: y-axis, number of microorganisms per m^3; x-axis, day of study
1-3) 1, 2 and 4 people, respectively
Solid lines--period when air-conditioners were not working; dash lines--period when they were working

c: 1-3) 1, 2 and 4 people, respectively
White bars--period when air-conditioners were not working; hatched bars--period when they were working

BG) background

It was previously noted that the degree of bacterial contamination of inside walls and equipment surfaces in a sealed room was greater when air-conditioning equipment was used (see Figure 1c) than when it was not used, other conditions being equal. As shown by the results of laboratory tests (Figure 2), accumulation of microorganisms on the inside surfaces, which was associated with decrease in concentration of bacterial aerosol, could apparently be related to the presence of flow of air because of operation of the air-conditioners. Intensive movement of air masses in a manned, confined room coul'd cause passage (settling) of microorganism-carrying particles from the bacterial aerosol to the interior surfaces [9], which confirms previously published data [7]. The results of our tests enabled us to establish that the level of bacterial contamination of interior surfaces of the pressurized room increases to the same extent with use of air-conditioning equipment in it and 2- and 4-fold increase in number of people in it (see Figure 1c, hatched bars 1, 2, 3).

Thus, as a result of these studies, determination was made of the intensity of accumulation of microorganisms in the atmosphere of a manned pressurized room and on its interior surfaces, as related to number of people and operation of air-conditioning equipment. It was shown that air-conditioning systems have the predominant effect on the process of formation of bacterial aerosol.

The obtained data can be used in designing life-support systems and developing measures to provide sanitary, hygienic and epidemic-free conditions for people working in confined, isolated quarters.

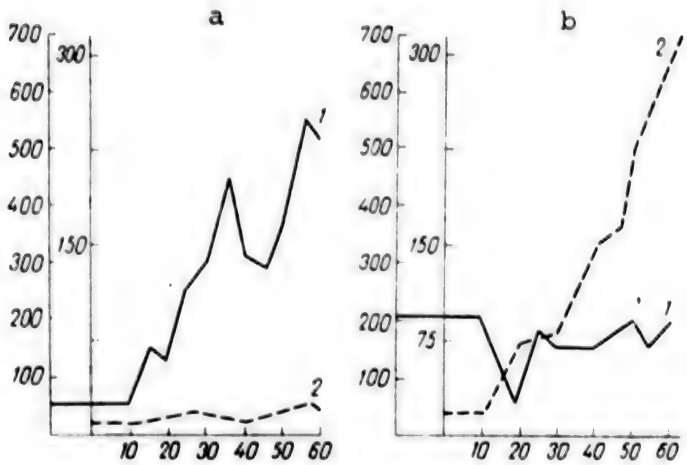

Figure 2. Dynamics of aerosol concentration (1) and quantity of microorganisms on interior surfaces (2) of isolated room when fan is off (a) and on (b)

X-axis, time (min) of collection of air samples with Krotov apparatus; y-axis, quantity of microorganisms per m^3 air

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NUTRITIONAL STATUS AS RELATED TO DIFFERENT WAYS OF USING EMERGENCY CARBOHYDRATE RATIONS

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[Article by I. G. Popov, P. A. Lozinskiy and I. A. Romanova]

[English abstract from source] Healthy male test subjects were allowed to consume a small-size contingency diet (300 g caramel) during 5 days of survival in a moderate climate in two modes: 1) uniform intake during 5 days or 2) consumption during the first 3 days and fasting during the remaining 2 days. The first mode proved more advantageous. This conclusion was drawn from evaluations of the general health status, body weight losses, carbohydrate, nitrogen, and mineral metabolism, ECG, and dynamometry.

[Text] As a rule, the crews of aircraft are limited in the food stowed in portable emergency supply packs (PES) to be used for "survival" after an emergency landing or splashdown. If the crew must stay in an unpopulated area for 3-5 days or more, it is possible to organize only low-calorie (sub-calorie) nutrition using the PES food supply [1]. The crew is immediately faced with the question of optimum tactics in utilizing the available food supply. Of course, the choice of a particular mealtime schedule in an emergency depends on a number of factors: total nutritional value of the emergency rations, expected time to be spent in the landing area until help arrives or they are evacuated, climate and geographic distinctions of landing area, nature of physical loads, presence or absence of potable water, etc. It is not easy to consider all of these factors to an equal extent at the early stage of the "survival" period. However, aircraft crews are compelled to make a decision at the first start of "emergency survival" conditions, on the basis of either recommendations provided in official instructions in the PES, or their own experience or information gleaned from other sources.

In spite of their importance, problems of nutrition in emergency situations have not yet been sufficiently worked on in the physiological and hygienic aspects. There are general recommendations in the literature which propose, for example, that the PES rations be used only when it is impossible to supplement supplies with local sources and that they be stretched over as long a period as possible; it is also recommended to take food in small portions [2].

On the whole, such recommendations are correct. However, for practical use it would be desirable for them to be more specific with regard to the schedule of emergency mealtimes and take into consideration the above-mentioned "survival" factors. For this, it is necessary, first of all, to have sufficiently extensive data on the dynamics of the nutritional status when using different types of emergency rations in the basic variants of mealtime schedules and under "survival" conditions of crews. Thus far, not enough such information has been published.

We submit here the results of a comparative evaluation of dynamics of nutritional status of subjects who used for 5 days the same low-calorie emergency rations containing only readily assimilated carbohydrates (300 g hard caramel candy), but with two different eating schedules. The first provided for intake of all the rations in the first 3 days followed by fasting for 2 days. In the second variant, the food supply was to be used in small portions over the entire 5 days.

Methods

For 5 days of our studies, the subjects' meals were organized on the following schedule. On the morning of the first day of the study, all subjects were given the standard preflight breakfast: 43 g protein, 46 g fat, 115 g carbohydrates with total energy value of about 1017 kcal. The foods contained in the breakfast weight about 505 g. In addition, they were given 200 g hot tea and 200 g fruit juice. The "flight" began 1.5 h after breakfast, and after another 2 h an "emergency landing" was announced. On the evening of the first day of the emergency situation, the 1st group of subjects (who consumed the rations for the 1st 3 days and then fasted for 2 days) took 40 g (144.8 kcal) caramels and 130 g caramel on each of the next 2 days. They received no food at all on the 4th and 5th days, but drank water. The 2d group of subjects (who stretched the rations over all 5 days), took 20 g caramel on the evening of the 1st day and 70 g for each of the next 4 days. On the first mealtime schedule, the subjects received 40 g (144.8 kcal) caramels for breakfast and supper and 50 g for lunch (181 kcal) on days 2 and 3. On the second schedule, they took 20 g (72.4 kcal) caramel for breakfast and supper and 30 g (108.6 kcal) for lunch on days 2-5. Thus, they took food at the usual hours and it was relatively uniformly distributed over breakfast, lunch and supper. The energy value of the entire emergency food supply, which consisted of 300 g caramel candy, constituted 1086 kcal (4545 kJ) [3]. Consequently, the 1st group of subjects had a food allowance on the 1st day that consisted of 1161.8 kcal (preflight breakfast 1017 kcal and 40 g caramel 144.8 kcal), and on the next 2 days it constituted 470.6 kcal/day in the form of 130 g caramel daily. The 2d group of subjects received 1089.4 kcal on the 1st day and 253.4 kcal/day for the next 4 days in the form of 70 g caramel daily. During the period of the simulated emergency situation drinking water was issued at the rate of 1 ℓ/day. Our test subjects were essentially healthy men 30-40 years of age. The subjects were in a temperate climate zone. Their energy expenditures were in the range of 3000-3200 kcal/day. The method used for evaluating their nutritional status is described in [4, 5].

Results and Discussion

Table 1 lists the results of studies of dynamics of the subjects' weight with use of the entire low-calorie emergency rations (300 g caramel) for the first

Table 1. Dynamics of subjects' weight on low-calorie carbohydrate rations used only for the first 3 days of an "emergency situation" ($n = 6$)

Subject	Ht., cm	Initial weight, kg	Weight status, Broca index, kg	Weight loss, kg (% in parentheses)						Wt. after 5 days, kg	Recommend. wt. according to A.A. Pokrovskiy, kg
				day in emergency situation					total 1st-5th days		
				low-calorie diet				total fast			
				1	2	3	1-3	4	5		
P-ev	178	84.50	+0.50	1.50 (1.78)	1.00 (2.96)	0.55 (3.61)	4.05 (1.61)	0.60 (1.12)	0.60 (1.99)		
M-ov	178	84.15	16.15	1.75 (2.08)	0.60 (2.79)	0.50 (3.14)	2.85 (2.53)	0.95 (4.50)	1.00 (6.20)		
S-ov	181	78.20	2.80	1.00 (1.28)	0.80 (2.30)	0.55 (3.01)	2.35 (2.71)	0.60 (3.77)	1.05 (5.12)		
K-ov	172	76.85	-1.85	1.15 (1.51)	1.20 (3.10)	0.50 (3.75)	2.85 (3.75)	0.40 (4.27)	1.17 (5.75)		
P-in	176	71.20	1.80	1.25 (1.63)	0.55 (2.43)	0.40 (2.96)	2.20 (2.96)	1.00 (4.31)	1.78 (8.69)		
K-ev	164	64.80	3.20	0.85	0.45	0.30	1.60	0.45	0.80		
M±m				1.26 ± 0.15 (1.61 ± 0.13)	0.77 ± 0.12 (2.60 ± 0.18)	0.50 ± 0.02 (3.25 ± 0.16)	2.52 ± 0.20 (3.25 ± 0.16)	0.67 ± 0.10 (4.11 ± 0.13)	1.02 ± 0.06 (5.45 ± 0.20)	4.21 ± 0.28 (5.15 ± 0.20)	

3 days followed by total fast for the next 2 days. Their weight dropped daily during all 5 days due to the change to a subcalorie (low-calorie) diet at first and then to a total fast (on the 4th and 5th days). In absolute values, the greatest weight loss in most subjects was observed on the 1st day of the "emergency situation" (1.26±0.15 kg), even though they consumed food with higher caloric value (preflight breakfast + 40 g caramel) than on the next 2 days (only 130 g/day caramel). Consequently, the caloric deficiency was lower on the 1st day than on the following ones. The reason for this is the more drastic reduction in food intake and volume of contents of gastrointestinal tract, as well as greater loss of fluid. On the 2d day, the change in weight was less marked than on the 1st day in most cases. Weight continued to drop on the 3d day (0.50±0.02 kg).

Individual differences in weight change were also greatest on the 1st day of the subcalorie diet, and on the 3d day they leveled off, being in the range of 0.4-0.5 kg. Weight loss in the first 3 days constituted 2.52±0.2 kg for the group of subjects, with individual differences ranging from 1.8 to 3.1 kg. In a percentile expression, weight loss reached 3.25±0.16% of the base level, ranging from 2.78 to 3.75%. In most cases, the subjects with higher initial weight lost more in 3 days. There was only one exception.

On the 4th day, when the subjects were fasting, weight loss increased appreciably in only 2 out of the 6 subjects. Considering the accuracy of the medical scale used, it can be considered that daily weight loss remained at the level found on the 3d day. However, the mean values did increase on the 4th day for the group as a whole. On the 5th day (or 2d day of total fast), weight loss was more significant than on the 3d and 4th days of the "emergency situation." Average weight loss in the group constituted 1.02±0.06 kg on the 5th day,

0.50±0.02 kg on the 3d and 0.67±0.10 kg on the 4th day. In most cases, weight loss was greater on the 5th day than the 2d. Consequently, with the change to a complete fast on the 4th and 5th days of the "emergency situation", the daily weight loss began to increase again due to the increased calorie deficiency and discontinued intake of food.

The 5-day weight loss in the "emergency situation" constituted for the group as a whole 4.21±0.28 kg (5.4±0.2%), with individual fluctuations in the range of 4.71-5.82% of initial weight. This can be evaluated as moderate weight reduction, far from the critical level of 40-50% that is hazardous to health and life [6].

When an identical diet was used under analogous conditions, but with uniform intake of caramel (or caramel and sugar; 20 g on the 1st evening and 70 g on each of the next 4 days), we observed the following: on the whole, 5-day weight loss constituted 3.76±0.09 kg, or 4.9±0.17%, with fluctuations from 4.68 to 5.70% of base weight [4]. Consequently, according to the average values, a uniform intake of the rations over a 5-day emergency period was associated with less significant weight loss. At the same time, weight loss on this schedule constituted 3.56±0.22% in the first 3 days (ranging from 2.71 to 4.34%), which exceeds insignificantly the above-mentioned analogous figures for weight loss when the same rations were consumed in 3 days, rather than 5. There was some tendency toward decrease in weight loss with intake of 130 g/day caramel on the 2d and 3d days of the "emergency situation," instead of 70 g/day.

On the 4th day of the study, when we gave out 70 g caramel, weight loss was in the range of 0.55-0.70 kg and reached 3.62-5.25% of initial value. At the same time, when the subjects began to fast, weight loss on the 4th day constituted 0.67-1.0 kg and reached 3.47-4.5% of initial value. Consequently, in this period the daily weight loss was already smaller with uniform intake of food supply. However, overall weight loss (as percentage of base weight) was even more significant than with intake of entire rations on the first 3 days and subsequent fasting.

On the 5th day of the study, with intake of 70 g caramel weight loss was in the range of 0.3-0.7 kg. Total loss on the 1st-5th days reached 4.9±0.17% with individual fluctuations from 4.68 to 5.46% of base weight. With uneven intake of rations, on the 5th day of the studies when the subjects had already fasted for 2 days, weight loss constituted 1.02±0.06 kg (from 0.8 to 1.2 kg), while overall 5-day loss reached 5.45±0.2% (from 4.71 to 5.93%) of initial level. Consequently, there was more significant loss of weight on the 5th day with irregular intake of food than on the 4th day.

By the end of the 5th day, weight loss (percentage of base value) with uneven intake of emergency rations was already greater than with even intake of the same rations over all 5 days.

Thus, weight loss (% of base value) in the first 3 days was relatively lower than when the entire emergency rations were consumed in this time (300 g caramel) than with uniform intake of food for 5 days. However, the situation changed by the end of the 5th day. Subjects who had used up the entire rations were compelled to fast on the 4th and 5th days, and they lost more weight as a whole in 5 days than those who divided the same rations evenly over the 5 days. Consequently, for the first 3 days there were advantages to faster

consumption of emergency rations, whereas by the end of the 5th day there were already some advantages to uniform intake of the low-calorie food supply.

The mealtime schedule involving intake of the entire carbohydrate food supply in the first 3 days creates different conditions for carbohydrate metabolism than in the case of uniform intake of these rations over all 5 days of the emergency situation. We could have expected a better blood sugar level on the first 3 days and a worse situation on the next 2 days of total fast in the case of uneven utilization of the food supply.

We used the glucose oxidase method, as modified by I. S. Balakhovskiy [5] to assay capillary blood glucose content, considering 69.3 to 80.7 mg% (70±10.7%) to be the normal concentration.

When the entire food supply was consumed on the first 3 days, blood glucose levels remained in the normal range, in the morning and evening, in most subjects. Sporadic hypoglycemic signs were noted on the 2d day in 3 subjects, in the morning and 1 in the evening, and on the 3d day only in the evening in 1 subject (in 3 others glucose concentration was at the bottom of the normal range). On the 4th day, hypoglycemia was found in 2 subjects in the morning and in all of them in the evening. Signs of hypoglycemia were observed in all subjects on the 5th day. On the other eating schedule, when the same food supply was taken uniformly, signs of hypoglycemia were also observed periodically for the first 3 days. Hypoglycemia was demonstrated even more often on the 4th and 5th days, but not in all subjects, and it was transient. The impression was gained that, with the change to fasting, carbohydrate metabolism became more intensive, while hypoglycemic signs appeared more often and more markedly. With uniform intake of even such small amounts of caramel as 70 g/day for 5 days, hypoglycemia was still observed less often than on the last 2 days with nonuniform intake of the food supply, when the subjects were on a complete fast. On the whole, with the nonuniform intake of emergency rations for the first 3 days, there was an insignificant advantage with regard to blood sugar level, but on the 4th and, particularly, 5th days, uniform intake of these rations had a better effect on this parameter. By the evening of the 1st day on the recovery diet, the signs of hypoglycemia disappeared in both groups of subjects.

In the case of subcalorie diet and total fast there is increased synthesis of ketone bodies due to depressed utilization of acetyl-CoA in the Krebs cycle. As a result, there is development of ketonemia and ketonuria [7]. Table 2 lists the results of assaying ketone body excretion in urine of the subjects. We used a modification of the method of Ember and Bonnamur [5]. With intake of an ordinary diet, ketone bodies were not demonstrable in urine. No ketone bodies were found on the first 3 days when the entire emergency rations were consumed. In the 2d group of subjects, who consumed less carbohydrates (70 g instead of 130 g caramel on the 2d and 3d days), ketone bodies began to appear on the 3d day, which is indicative of earlier development of carbohydrate deficiency and earlier ketone synthesis. On the 4th and, particularly, 5th days, after changing to a total fast, all subjects excreted ketone bodies. Among those who continued to consume small amounts (70 g/day) carbohydrates on the 4th and 5th days no excretion was demonstrated. The differences between the two groups in ketone body excretion were particularly noticeable on the 5th day of the study. The data listed in Table 2 warrant the belief that ketone

synthesis increased drastically in the 1st group of subjects, with the change to a total fast, already on the 1st day of the fast and became significant on the 2d day.

Table 2. Excretion of ketone bodies in urine of subjects consuming emergency carbohydrate rations (300 g/caramel) in different ways, g/day

Group	Subject	Day of "emergency situation"					First day of recovery period diet
		1	2	3	4	5	
First (entire food supply consumed on 1st-3d days, fast on 4th-5th days)	P-ev	None	None	None	0,530	2,190	None
	M-ov	»	»	»	0,305	1,925	"
	S-ov	»	»	»	0,200	2,320	"
	K-ov	»	»	»	0,490	2,800	"
	P-in	»	»	»	0,345	2,445	"
	K-ev	»	»	»	0,368	2,994	"
Second (uniform intake of food supply on 1st-5th days)	L-y	None	None	None	0,226	0,411	"
	P-ov	»	»	0,258	None	0,416	"
	Kh-ov	»	»	0,157	0,387	None	"
	L-ich	»	»	None	None	0,271	"
	K-ov	»	»	»	»	None	"
	V-ev	»	»	0,235	0,371	»	"
	K-ev	»	»	None	None	»	"

With uniform intake of small amounts of carbohydrates, ketonuria appeared sooner (on the 3d day) in some subjects, but increased less on the 4th and 5th days and not in all subjects nor to the same extent as in the 1st group who changed to a total fast. Thus, the uniform mode of using emergency carbohydrate rations (even in such a small amount as 70 g) was associated with a less marked process of ketone synthesis than when consuming the entire emergency food supply on the first 3 days with subsequent fasting. We were impressed by the fact that the signs of ketonuria disappeared on the very 1st day of the recovery period, when urine was collected after the subjects changed to a diet rich in readily assimilated carbohydrates with limited fat and protein content. These data are in agreement, to some extent, with the results of assaying blood sugar, where signs of hypoglycemia were more marked on the 4th-5th days with nonuniform intake of the food supply.

General health status, well-being and work capacity can be rated as satisfactory for the first 3 days on the subcalorie diet, according to medical findings and the subjects' own conclusions. On the 1st day of the "emergency situation" the subjects observed appearance of hunger at the time of their usually scheduled meal (in this case, lunch). The hunger sensation did not bother them much and was abated by intake of a few sips of cold water. In the evening, at the time for their usual supper, the feeling of hunger became stronger. Intake of 40 g caramel and a glass of water eliminated this sensation to a significant degree, as well as the related discomfort. During the 2d and 3d days, the subjects reported periodic general weakness, worsening of well-being and work capacity. The time of onset of these signs, as well as their duration and severity, varied in different individuals. Intake of caramel at the usual time for breakfast, lunch and supper dulled significantly or even removed the sensation of hunger and improved well-being.

Determination of hand strength by the dynamometric method revealed insignificant worsening of this parameter on the first 3 days of the low-calorie diet. Before our tests, hand strength was in the range of 55.3±1.93 kg for the right hand and 52.7±1.93 kg for the left. On the 1st day of the low-calorie diet, this parameter constituted 54.8±2.58 kg (right hand) and 52.0±1.4 kg (left); on the 2d day the figures were 54.2±0.14 (right) and 50.2±0.81 kg (left); on the 3d day, 52.2±2.75 (right) and 50.7±1.45 kg (left). With the change to the fast on the 4th day there was further insignificant, but more noticeable decline of this parameter to 53.7±2.58 (right hand) and 48.5±1.78 kg (left). But on the 5th day (or 2d day of fast), strength of hands increased somewhat, to 54.8±2.75 kg (right hand) and 51.7±1.45 kg (left), i.e., to the level of the 1st day on the low-calorie diet, which could be a reflection of development of general excitation on the basis of the stress of hunger. On the 3d day of recovery diet, hand strength was virtually on the initial level or even higher: 56.8±2.9 kg (right hand) and 53.0±2.26 kg (left). Backbone strength constituted 121.0± 7.25 kg before the tests, 118.0±8.0 kg on the 1st day of the low-calorie diet, 114.8±7.6 kg on the 2d day and 108.8±4.6 kg on the 3d, i.e., it gradually diminished. On the 4th day of the emergency situation, with the change to fasting, it constituted 104.5±5.4 kg, but on the 5th day it increased to 108.2± 6.1 kg, which corresponded to the level on the 3d day of the low-calorie diet. Evidently, this should also be attributed to the stress reaction to a total fast.

Evaluation of the subjects' EKG failed to demonstrate pathological signs. On the whole, the signs were the same as with other variants of low-calorie diets [4, 5]. Blood pressure periodically dropped by 5-15 mm Hg, while pulse became 10-15/min slower than initially.

With the change to total fast on the 4th and, particularly, 5th days of the "emergency situation," all subjects reported noticeable worsening of their general condition: periodic weakness, stronger and longer sensations of hunger, signs of anxiety because of the impossibility of taking even a small amount of "any" food.

During the fasting period, the EKG did not change appreciable, but in some subjects the T_2 wave amplitude diminished somewhat while the QT segment had a tendency toward widening. These changes could have been due to changes in electrolyte metabolism against the background of demineralization of the body.

A comparison of the above data to analogous parameters in the case of uniform nutrition [4] leads us to conclude that no appreciable differences were observed on the first 3 days. However, on the 4th-5th day, under fasting conditions, the subjective state, particularly with regard to sensations of hunger and development of general weakness, was poorer than on the low-calorie diet. At the final stage of the "survival" situation, the subjects preferred uniform intake of the food supply, without fasting.

Examination of excretion of potassium, sodium, chlorine and phosphorus in urine showed a decline in excretion of these macroelements in all subjects with nonuniform consumption of the rations for 5 days. Only potassium and sodium excretion increased somewhat on the 5th day, as compared to the 4th (Table 3). Judging by the mean figures, potassium and chlorine excretion was below the physiological norm starting on the 2d day, sodium excretion was below this

value already on the 1st day, while phosphorus was below on the 4th day, which is attributable to their negative nutritional balance. Initially, macroelement excretion was in the "normal" range.

Table 3. Dynamics of excretion of macroelements in urine of subjects on different schedules of intake of low-calorie "emergency rations" (300 g caramel)

Diet	Macroelement levels in 24-h urine, μg/day			
	potassium	sodium	chlorine	phosphorus
	1st group of subjects (n = 6)			
Ordinary	2284±213	4100±383	7907±739	1119±105
Low-calorie rations consumed on 1st-3d days:				
1st day	1480±138	2652±248	5372±502	706±66
2d day	1169±109	985±92	2483±232	722±67
3d day	890±83	417±39	1129±105	703±66
4th day (fast)	805±75	379±35	745±70	526±50
5th day "	902±84	489±46	517±48	439±41
	2d group of subjects (n = 7)			
Ordinary	2278±191	3653±388	8083±612	889±87
Low-calorie rations consumed uniformly on 1st-5th days:				
1st day	2070±142	2470±192	5322±582	827±76
2d day	1160±101	2638±870	2638±42	568±69
3d day	1103±152	619±140	1388±139	679±109
4th day	1001±147	528±105	1030±10	573±219
5th day	1012±127	406±73	622±167	406±32
Physiological norm on ordinary diet according to textbooks edited by:				
A. A. Pokrovskiy, 1964	to 2000	3 000—12 000	4 500—9 000	1 000—2 000
A. I. Vorob'yev, 1982	1 500—3 000	3 000—6 000	600—700 mg%	600—1 2000

In the tests with uniform intake of food supply, the findings were quite similar [4]. The only difference was that there was virtually no increase in potassium excretion on the 5th day, which could be due to a less marked acidotic change. Starting on the 2d day, potassium, chlorine and phosphorine excretion was below the physiological norm, but on the 3d day phosphorus excretion returned to the bottom of the normal range, while excretion of sodium was below the norm already on the 1st day of the "emergency situation."

Demineralization, which occurred in the course of our studies, was not associated with any appreciable changes in subjective condition, but some of the demonstrated EKG changes could have still been due to a change in optimum macroelement status.

The shortage of macroelements we studied could also have made its contribution to the periodically appearing general weakness and decline of work capacity. A comparison of macroelement excretion on both eating schedules with the emergency

rations revealed a tendency toward greater excretion of potassium and chlorine in urine on the 4th and 5th days, and the same for sodium and phosphorus on the 4th day of uniform intake of food. This could be due to the specifics of macroelement turnover in the case of continuing intake of low-calorie diet, as compared to change to fasting conditions. On the whole, we failed to demonstrate any appreciable differences in excretion of macroelements between the two schedules of consuming emergency food supplies.

With nonuniform intake of the carbohydrate diet, total nitrogen excretion in urine decreased already on the 1st day of low-calorie diet (Table 4). On the 2d and 3d days, when there was no protein at all in the diet, there was a drastic decrease in nitrogen excretion. When on the total fast, such a drastic decline in nitrogen excretion is usually not observed on the first days [8]. Evidently, in this instance, carbohydrates had a protein-conserving effect. On the 4th day, when the subjects began a total fast, there was appreciable increase in nitrogen excretion due to activation of gluconeogenesis at the expense of nitrogen-containing substances. This confirms the above-mentioned protein-conserving effect of readily assimilated carbohydrates. On the 5th day (or 2d day of fast), nitrogen excretion continued to increase, although the increase was insignificant in comparison to the 4th day. In the 5 days of the emergency situation, total nitrogen excretion constituted 52.68±0.81 g, while total intake of nitrogen with food was about 6.88 g in the same period (emergency rations and preflight breakfast). In this time, extrarenal loss of nitrogen [9] constituted 6.34±0.26 g. Consequently, the negative nitrogen balance reached 52.3±0.81 g in 5 days, which is about 5.23% of the total nitrogen contained in the human body. This is much less than the critical level, which constitutes 50% with breakdown of 40-45% of body proteins [6]. All this warrants the belief that, by the end of the 5th day, only the incipient stage of protein deficiency was present.

Table 4. Total nitrogen excretion in 24-h urine before, during and after nonuniform intake of low-calorie "emergency rations" consisting of carbohydrates (g)

Subjects	Days of ordinary diet		Day of emergency situation							Days after emergency rations			Negative nitrogen balance, day	
			low-calorie diet				total fast			recovery diet		ordinary		
	1	2	1	2	3	1-3	4	5	1-5	1	3	5	1-3	1-5
P-ev	15,7	15,3	10,65	8,53	8,04	27,22	11,93	12,20	51,35	9,65	12,35	15,55	24,54	51,40
M-ov	15,00	16,30	11,87	9,26	9,14	30,27	10,40	12,25	52,92	12,44	15,36	15,40	27,56	52,92
S-ov	12,90	13,45	13,23	8,38	8,10	29,71	11,00	11,74	52,45	11,20	12,03	13,61	26,73	52,01
K-ov	14,10	13,50	12,93	8,10	8,04	29,07	12,89	13,20	55,16	12,43	12,90	14,36	26,01	54,59
P-in	12,90	13,70	12,27	9,45	8,01	29,73	11,43	12,93	54,06	10,98	14,60	15,34	26,54	53,27
K-ev	13,00	13,73	12,90	8,14	7,90	28,94	10,45	11,73	50,12	12,30	12,86	14,23	25,30	49,59
M	13,93	14,33	12,31	8,64	8,20	29,16	11,34	12,34	52,68	11,50	13,35	14,75	26,11	52,30
$\pm m$	0,45	0,46	0,42	0,22	0,20	0,49	0,40	0,24	0,81	0,45	0,49	0,31	0,49	0,81

With uniform intake of the food supply, the negative nitrogen balance constituted 49.78±0.70 g by the end of the 5th day, which is about 4.98% of all nitrogen in the body. In the case of total fast on the 5th day, the negative protein balance constituted 5.9% of initial status [8]. Comparatively speaking, it should be noted that, with uniform intake of the food supply, half the subjects presented further decline of nitrogen excretion on the 4th day, as compared to the 3d, while the other half demonstrated an insignificant increase [4]. On the 5th day, nitrogen excretion was lower in all subjects than on the 4th and, in virtually all of them, it was lower than on the 3d. Consequently, there are distinct differences in dynamics of nitrogen excretion in urine on the 4th and 5th days between the two mealtime schedules analyzed. From the standpoint of prevention of disturbances in protein metabolism, uniform intake of food may be evaluated as being more beneficial.

Development of the process of protein deficiency is confirmed by the results of testing urea and ammonia excretion. With an ordinary diet, urea excretion was on the level of 27.63±0.95 g/day, while the share of urea nitrogen in total nitrogen constituted 90±0.97%. On the 3d day of the low-calorie diet, these parameters dropped to 12.12±26 g/day and 69±0.81%, and on the 5th, to 13.22± 0.51 g/day and 50±0.67%, respectively. Such a decrease in share of urea nitrogen in total urine nitrogen, with some increase in its excretion in urine, is indicative of progression of the process of protein deficiency during the period when no food was taken, as a result of intensification of utilization of endogenous protein for gluconeogenesis [10, 11]. By the end of the 3d day, ammonia excretion decreased to 0.790±0.01 g/day, while the share of ammonia nitrogen constituted 7.94±0.20% of total nitrogen. In the base period, these parameters constituted 0.815±0.008 g/day and 4.67±0.17%, respectively. By the end of the 5th day, ammonia excretion constituted 1.284±0.43 g/day and the relative indicator of its excretion was 8.60±0.18%. On the 3d day of the recovery diet, the parameters of ammonia excretion returned to virtually the base level.

Creatinine excretion in urine constituted 1.79±0.32 g/day in the initial period, 1.63±0.027 g/day on the 3d day of low-calorie diet and 1.60±0.023 g/day at the end of the 5th day. There was a return to virtually the base status on the 3d day of the recovery period. Such dynamics are indicative of insignificant change in muscle mass.

With uniform intake of food supply, urea excretion was somewhat lower by the end of the 3d day, constituting 11.75±0.44 g/day and the relative indicator being 59.30±0.56%, which is indicative of more marked processes of protein and calorie deficiency. By the end of the 5th day, urea excretion dropped to 9.75±0.29 g/day, with relative indicator of 52.9±0.84%. Consequently, by the end of the 5th day, the situation changed in favor of uniform intake of food supply, due to the more marked process of protein deficiency in the period of the 4th-5th days with nonuniform intake of the emergency food supply. Ammonia excretion under the same conditions of utilizing the emergency food supply constituted 0.916±0.036 g/day on the 3d day (relative indicator 8.16-0.19%) and 0.844±0.028 (relative indicator 8.13%) on the 5th day, which is indicative of more uniform development and less severe starvation than when the rations were consumed in the first 3 days and the subjects fasted for the next days. Creatinine excretion constituted 1.89±0.05 g/day in the base period,

1.80±0.04 g/day on the 3d day of the low-calorie diet, 1.75±0.014 g/day on the 5th day and 1.87±0.017 g/day on the 5th day of the recovery period. Consequently, there was no appreciable reduction of muscle mass.

Thus, judging by the indicators of nitrogen metabolism, for the first 3 days there was some advantage in consuming the entire food supply in this period due to the relatively greater intake of carbohydrates. By the end of the 5th day, there was some advantage to uniform intake of the food supply, when the subjects were not totally fasting. The negative nitrogen balance, which is viewed as a general indicator, was higher with nonuniform consumption of food supplies, which must be indicative of more intensive nitrogen metabolism.

These studies enable us to conclude that, in cases when it is difficult or impossible to predict the duration of a "survival" situation, it is wiser to make uniform use of the low-calorie, small-sized food supply over a period of 5 days of the emergency situation. The results of objective examination of dynamics of nutritional status, health, work capacity and subjective evaluations by our subjects indicate that one should avoid even brief total fasts in the second half of an emergency situation period. When there is stable contact with rescue organizations and complete certainty of getting help within the first 3 days, one does not have to conserve food, since this reduces the calorie deficiency.

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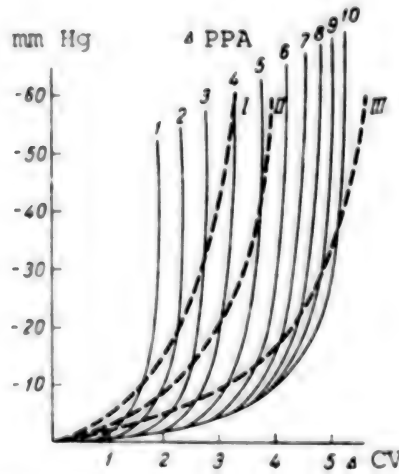
NOMOGRAM FOR DEMONSTRATING CHANGE IN CENTRAL VENOUS AND PULMONARY ARTERY PRESSURE DURING DECOMPRESSION OF DIFFERENT PARTS OF THE BODY

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 3, May-Jun 84 (manuscript received 4 Mar 83) pp 89-90

[Article by V. Ye. Katkov and V. V. Rumyantsev]

[Text] Different series of comprehensive studies were made of the effects of negative pressure (NP) on different parts of the human body [1-4]: local NP to both legs (LNP_I), NP to abdominal region (LNP_{II}) and NP to the bottom half of the human body (LBNP). In essence, the effect of this factor on central circulation was investigated, in particular, on such of its important parameters as central venous pressure (CVP) and pressure in the pulmonary artery (PPA). For convenience in evaluating the effect of NP, a nomogram is proposed, which is plotted from experimental data, and it is illustrated in the Figure. The changes in CVP are plotted on the x-axis and decompression modes on the y-axis, and the latter were virtually limited to -60 mm Hg. Curve I illustrates the result of using LNP_I, curve II the effect of LNP_{II} and curve III, LBNP. The rectilinear coordinate grid shows changes in PPA. At the same time, one can see that the coordinate curves ΔPPA show asymptotic contraction, which enables us to refer to maximum changes possible with use of NP over all regions of the human body. Having selected change in any parameter as the base, one can determine change in another parameter from the nomogram, as well as the modes required for NP to different areas. For example, a 3 mm Hg change in CVP can be obtained by using 37 mm Hg LNP_I, 20 mm Hg LNP_{II} and 10 mm Hg LBNP. This will result in PPA change of 3.4, 3.7 and 4.5 mm Hg, respectively. One can proceed analogously from the need to elicit a specific change in PPA. We are not furnishing the PPA change for LBNP modes exceeding -40 mm Hg, but this function can be extrapolated. In our opinion, the submitted



Nomogram for determination of change in CVP (in mm Hg) and PPA (in mm Hg) during decompression (y-axis) of different parts of the body. Explanation given in the text.

nomogram may be helpful to researchers concerned with the study of physiological effects on man of NP.

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BRIEF REPORTS

UDC: 616.151.5-07.616.155.34]-02:612.014.41

DEPENDENCE OF BLOOD COAGULATING AND FIBRINOLYTIC SYSTEMS ON FUNCTIONAL STATE OF LYSOSOMAL SYSTEM OF NEUTROPHIL LEUKOCYTES DURING EXPOSURE OF THE BODY TO LOW BAROMETRIC PRESSURE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 3, May-Jun 84 (manuscript received 22 Feb 83) pp 90-92

[Article by N. V. Lunina and A. F. Poltavskiy]

[Text] Typical changes are observed in the blood system when man and animals are exposed to low barometric pressure, and they are important to the body's adaptation to changing environmental conditions. There is stimulation of myelopoiesis; neutrophilia, lymphopenia and eosinophenia are noted in peripheral blood [1, 2].

Animal experiments have shown that, when the body is exposed to noninfectious stressors, in particular, acute loss of blood, not only is there development of absolute neutrophil leukocytosis, but there is a decrease in number of neutrophil leukocyte lysosomes [3].

It was previously established that, under the influence of low barometric pressure, animals develop neutrophil leukocytosis due to activation of myelopoiesis. At the same time, there is decrease in number of lysosomes of neutrophil leukocytes, which reaches a maximum on the 2d-3d day and reverts to the base level on the 5th day [4].

Our objective here was to investigate the possible correlation between decrease in number of lysosomes in neutrophils and change in activity of blood clotting and fibrinolytic systems when animals are exposed to low barometric pressure.

For this purpose, we assayed in blood plasma the lysosomal marker enzyme, cathepsin D, which enables us to assess the functional activity of lysosomes [5, 6] and parameters of blood clotting and fibrinolytic systems.

It is known from the literature that neutrophils are involved in blood-coagulating processes [7]. However, previously authors did not relate the effect of leukocytes on blood clotting and fibrinolysis to any neutrophil structures.

Methods

Experiments were conducted on 60 rabbits of both sexes weighing 2 to 3.5 kg. The animals were exposed once, for 1 h, to a pressure of 304 mm Hg in a

ventilated pressure chamber. Soda lime was used for absorption of CO_2 and water vapor. We measured cathepsin D activity [8] in the animals, blood clotting time [9], plasma recalcification time [10], prothrombin uptake [11], activity of prothrombin complex factors [12], concentration of fibrinogen [13], activity of fibrin-stabilizing factor [14], thrombin time [15] and fibrinolytic activity of whole blood [16]. The parameters of blood clotting and fibrinolytic systems were measured before the experiment, then 1, 2, 3, 4 and 5 days after i., while cathepsin D was assayed 3 h after exposure.

Effect of low barometric pressure on parameters of blood clotting and fibrinolytic systems (M±m)

Parameter	Time of test					
	before experim. (control)	postexperiment day				
		1	2	3	4	5
Clotting time, s	288,0±10,2	211,0±10,0	179,2±7,1	192,0±12,5	254,6±9,9	289,8±10,3
P		<0,001	<0,001	0,001	<0,05	>0,5
Recalcification time, s	91,0±3,4	73,0±5,7	66,5±6,0	78,5±3,1	88,0±3,2	91,2±3,2
P		<0,01	<0,01	<0,01	>0,5	>0,5
Prothrombin uptake, %	100,4±7,5	69,2±3,6	45,3±3,2	75,0±3,7	89,9±3,9	101,2±2,4
P		<0,001	<0,001	<0,001	<0,02	>0,5
Prothrombin index, %	65,6±1,0	77,6±4,4	90,5±4,0	95,9±3,5	85,2±3,5	65,4±0,8
P		<0,05	<0,001	<0,001	<0,001	>0,5
Fibrinogen concentration,%	163,9±11,0	205,2±13,4	227,2±11,1	212,2±10,1	196,2±10,0	166,0±10,8
P		<0,05	<0,001	<0,001	<0,05	>0,5
Fibrin-stabilizing factor, s	74,1±1,1	51,9±2,1	44,4±1,5	59,0±1,3	70,5±1,1	74,0±1,1
P		<0,001	<0,001	<0,001	<0,05	>0,5
Thrombin time, s	25,2±0,2	25,0±0,2	24,9±0,2	24,7±0,3	24,9±0,2	25,2±0,2
P		>0,5	>0,5	>0,5	>0,5	>0,5
Fibrinolytic activity, %	6,0±0,4	8,9±1,0	11,5±0,9	10,3±0,8	7,6±0,7	6,3±0,5
P		<0,02	<0,001	<0,001	<0,05	>0,5

Results and Discussion

The results of our study, which are listed in the Table, indicate that, already 3 h after exposure of animals to low barometirc pressure, activity of lysosomal enzyme increased and continued to grow at subsequent stages of our study, reaching a maximum on the 3d day (0.354±0.11). On the 5th day, cathepsin D activity did not differ from base values (0.0006±0.0001).

Examination of coagulating and fibrinolytic systems (see Table) showed that there was considerable reduction of clotting time, particularly on the 2d day after exposure. Thereafter (3d-4th days), clotting time gradually increased and was restored to the base level on the 5th day. The nature of changes in recalcification time was similar.

On the first 4 postexperimental days there was decrease in prothrombin utilization, with a maximum on the 2d day (by 55%) and return to base level on the 5th day. The increase in activity of prothrombin complex factors presented the same dynamics. Fibrinogen concentration increased at the same times, but reverted to the initial level on the 5th day. A decrease in activity of fibrin-stabilizing factor also started after 1 day, and it was the most marked (by 40%) on the 2d day. Its activity did not differ from base value on the 5th day. Thrombin time did not change at any stage of the studies.

Increase in whole-blood fibrinolytic activity was demonstrated 1 day after exposure with a maximum increase (by 90%) on the 2d day and restoration of base level on the 5th day.

Thus, the experimental results are indicative of activation of blood clotting and fibrinolysis, which was the most marked on the 2d-3d day after exposure. At the same times, we also observed increase in activity of plasma lysosomal cathepsin D, as well as the previously demonstrated [4] decrease in number of lysosomes in neutrophils.

The demonstrated reactions of blood coagulating and fibrinolysis systems when animals were exposed to low barometric pressure could be attributed to changes in the lysosomal system of neutrophils, since there has been in vitro demonstration of activation by neutrophil lysosome enzymes of the Hageman factor [17], which controls coagulation, fibrinolysis and kininogenesis systems [18].

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SIMULATION OF PHYSIOLOGICAL EFFECTS OF NEGATIVE PRESSURE ON MAN

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 3, May-Jun 84 (manuscript received 25 Nov 82) pp 92-93

[Article by V. V. Rumyantsev and V. Ye. Katkov]

[Text] It was previously shown that pressure in the pulmonary artery (PPA) and central venous pressure (CVP) are informative indicators for evaluation of the effects of lower body negative pressure (LBNP) and local negative pressure (LNP) to both legs (LNP_1) and the abdominal region (LNP_2) [1-5].

Use of these indicators made it possible to develop a mathematical model that describes changes in central circulation during decompression of different parts of the human body.

Some similarity of reactions of PPA and CVP to decompression was noted with use of LBNP in the range of 0 to -60 mm Hg. The function is nonlinear, and at high levels of rarefaction both PPA and CVP tended toward stabilization of a level, which was usually achieved at p = -60 to -80 mm Hg (Figure 1).

Consequently, the boundary conditions can be expressed as follows:

$$P_T|_{p=0} = P_И \;\&\; P_T|_{p\to\infty} = P_0, \qquad (1)$$

where P_T is current pressure, $P_И$ is initial pressure and P_0 is end pressure.

Proceeding from the boundary conditions, pressure as a function of degree of decompression can be expressed as an equation, $P_T = (P_И - P_0)\cdot f(p) + P_0$, where function $f(p)$ is defined as $f(p) \to 0$ with $p \to -\infty$ and $f(p) = 1$ with $p = 0$. PPA as a function of decompression in the practically relevant range of 0 to -30 mm Hg is described by the formula, $P_T = P\cdot e^{\alpha p}$ [2, 3]. Let us take $f(p) = e^{\kappa\alpha p}$, where κ and α are certain parameters, then formula (1) will acquire the following appearance:

$$P_T = (P_И - P_0)\, e^{\kappa\alpha p} + P_0. \qquad (2)$$

Figure 2 illustrates the results of processing experimental data. To compare results in the background period and on the 2d, 4th and 7th days of AOH

[antiorthostatic--head tilted down--hypokinesia], the changes in PPA and CVP were expressed as percentages.

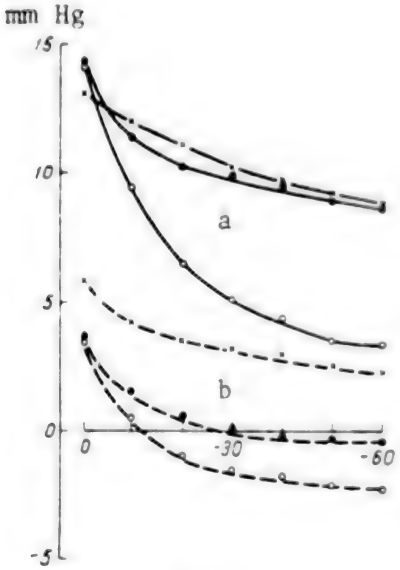

Figure 1.
PPA (a) and CVP (b) curves during decompression of different parts of the body

Here and in Figure 2:
X-axis, rarefaction (mm Hg)
White circles LBNP, black LNP_2 and x's LNP_1

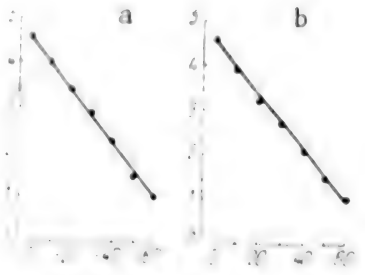

Figure 2.
Natural logarithm of relative pressure change as a function of degree of rarefaction under effect of LBNP

a) $PPA\left(\ln\frac{P_T - P_n}{P_H - P_n}\ 100\right)$;

b) $CVP\left(\ln\frac{P_T - P_0}{P_H - P_0}\right)$.

The data are submitted as the group average, where α is 0.03 and $\kappa = 2$.

Analysis of the pressure curves in the background period and at different stages of AOH revealed that formula (2) is valid for all cases, P_H and P_0 undergoing changes as a function of duration of AOH. This enables us to discuss quantitative evaluation of hemodynamics, and if conditioning is used with the means of preventing the adverse effects of weightlessness, one can assess the beneficial effects of conditioning according to adequacy of parameters in formula (1) and even express them quantitatively.

Consequently, in view of the same functional distinctions of surface vessels of the lower extremities, we can expect that the general law (2) will prevail under the effect of LNP to the leg, the only difference being in value of parameters. Analysis of experimental data revealed that function (2) is valid in this case also, but coefficient κ equals 0.42, which enabled us to consider it as an indicator of coverage of LNP. As was to be expected, a change in cardiac output was found to be proportionate to κ at the corresponding LNP and LBNP modes.

It should be noted that, in the case of LBNP and LNP to the leg, P_0 had the same value.

Coefficient α, which ranged from 0.15 to 0.4 in the group, is in our opinion a characteristic of individual differences.

Analysis of pressure curves with LNP_2 (area of hydrostatic neutral point) revealed that the pattern defined by formula (2) is valid for PPA and CVP, regardless of duration of AOH; the value of $\kappa\alpha$ in the group ranged from 0.03 to 0.15, while that of P_0 indicated that the maximum pressure is achieved at decompression of -70 to -80 mm Hg.

Formula (2) can be reduced to $P = P_{\text{н}}e^{\kappa\alpha p} + P_0(1 - e^{\kappa\alpha p})$. Evidently, the first term in this equation reflects changes in geometry of the lumen as a function of transmural pressure and the second, the changing vascular tonus. The fact that P_0 is identical with LBNP and LNP to the leg can serve as a confirmation of this.

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INDIVIDUAL DISTINCTIONS OF HUMAN SLEEPING RESPIRATION AT ALTITUDE OF 4200 METERS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 3, May-Jun 84 (manuscript received 7 Jan 83) pp 93-95

[Article by Ye. P. Gora]

[Text] The study of respiration during sleep under hypoxic conditions makes it possible to investigate more thoroughly the mechanisms of adaptation [1-7].

Studies of physiology of sleep under normal conditions establish a relationship between different sleep phases and specific nature of breathing [8, 9]. In a drowsy state, respiration is often periodic; during slow deep sleep it is rhythmic and there is attenuation of pulmonary ventilation. The stage of rapid eye movement (REM) corresponds to some increase in ventilation with nonrhythmic breathing [10]. At the present time, we still do not have a clearcut idea about the relationship between different phases of sleep and the specific nature of respiration at high altitudes.

Our objective here was to study the individual distinctions of change in respiration during nocturnal sleep at the first stage of adaptation to hypoxia.

Methods

Nine essentially healthy men 19 to 48 years of age participated in this study. Three of them were physicians who knew the purpose of the study.

Three subjects at a time slept for an average of 7 h for 3 successive nights in a pressure chamber at an "altitude" of 4200 m (450 mm Hg). They were "brought down to the ground" every morning. In the daytime, they were engaged in their professional duties.

While sleeping at "high altitude," we continuously recorded the subjects' pneumogram, EEG, EKG, electromyogram (EMG) and electrooculogram (EOG) on a 16-channel electroencephalograph. After waking and "descending" from 4200 m, the subjects reported on their well-being.

Results and Discussion

The same types of respiration were recorded in the subjects while sleeping at "an altitude" of 4200 m as have been described in [8-10]. However, there was considerably more marked periodic, "grouped" respiration, consisting of

groups of 3 (less often 2-4) respiratory cycles with 7 to 18 s pauses between them.

It was possible to divide the subjects into three groups, in accordance with their individual respiratory distinctions (see Table).

Distribution of different types of respiration as a function of time in subjects while asleep in pressure chamber at an altitude of 4200 m

Group	Subjects	Night	Type of respiration during sleep at "4200 m"					
			regular		irregular		periodic	
			min	%	min	%	min	%
1	Z-v	1st	89	21,2	178	42,4	153	36,4
		2d	145	37,6	147	39,1	94	24,3
	K-v	2d	92	19,2	161	33,5	227	47,3
		3d	120	30,4	135	34,2	140	35,4
	Zh-v	1st	27	6,4	102	24,3	291	69,3
		2d	223	53,1	129	30,7	68	16,2
2	Zv-v	1st	103	24,5	300	71,4	17	4,1
		3d	64	24,6	41	15,8	155	59,6
	U-d	1st	4	1,0	336	83,0	65	16,0
		3d	15	3,6	334	79,5	71	16,9
3	L-u	1st	114	37,3	95	31,0	97	31,7
		2d	71	16,9	166	39,5	183	43,6
	Ch-v	1st	5	1,2	156	37,1	259	61,7
		3d	—	—	85	20,2	335	79,8
	Ch-kov	2d	33	7,9	180	42,9	207	49,2
		3d	26	6,2	89	21,2	305	72,6
	Sh-v	2d	32	7,9	142	35,0	231	57,1
		3d	—	—	112	26,7	308	73,3
$M \pm m$			72±19,9	17,6	160±28,0	39,0	178±32,5	43,4

In representatives of the 1st group, which presented more stable rhythmic breathing while awake before the "ascent," the same type of breathing also persisted for a considerable time while asleep at "high altitude." Their rhythmic respiration coincided with deep slow sleep. In the same group of subjects, with initially rhythmic respiration and marked variations of amplitude, periodic breathing during sleep usually appeared after motor activity, with change from the rapid sleep phase to the somnolent phase.

There was prevalence of respiration of irregular depth and rhythm in subjects of the 2d group while sleeping at "an altitude" of 4200 m. According to the EEG data, this type of respiration coincided mostly with the REM phase, as well as increased pulmonary ventilation. However, it was also observed episodically in other sleep phases.

In the 3d group of subjects, the slow sleep phase was consistently associated with periodic breathing.

We observed different individual changes in types of respiration.

For example, in the 1st group, during the 2d and 3d nights at an "altitude" of 4200 m, the time of periodic respiration in deep sleep (stages III-IV of slow sleep) decreased by an average of 25.7% (11.9-53.1%), as compared to the 1st night due to a corresponding increase in regular breathing time.

No deviations of respiration dynamics from the 1st to 3d nights were noted in the 2d group of subjects.

In the 3d group, hypoxia had an increasing effect on respiration of sleeping subjects, as indicated by the increase in duration of periodic respiration by 16.2-23.4% form the first to 3d nights.

Thus, each sleep phase at low barometric pressure corresponds to a specific type of breathing characterizing the distinctions of the mechanism of its regulation, in spite of some individual differences.

During sleep under normal conditions, suprabulbar influences on the respiratory center are weaker, and the humoral mechanism of respiratory regulation moves to the fore [11]. It is manifested with particular force during sleep under hypoxic conditions. On the one hand, there is an increase in sensitivity of the respiratory center to CO_2; on the other hand, sleep "dulls" the hypoxic effect that determines increase in this sensitivity.

Such changes in regulation of respiration occurs differently in healthy people, and this apparently determines the individual distinctions of structure of breathing and its changes during sleep "at an altitude" of 4200 m at the early stage of adaptation to hypoxia.

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ARTIFICIAL MINERALIZATION OF GLACIER MELT TO BE USED FOR DRINKING DURING MOUNTAIN EXPEDITIONS AT HIGH ALTITUDES

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[Article by M. I. Shikina, T. I. Aladinskaya, S. V. Chizhov, Yu. Ye. Sinyak and S. P. Orlovskiy]

[Text] Glacier melt is similar in its physicochemical composition to distilled water, and it does not contain the physiologically essential minerals and trace elements, such as calcium, magnesium, potassium, sodium, sulfates, chlorides, fluorine, iodine, etc., that are inherent in natural potable water. This water is deficient in organoleptic properties and salt composition, so that it is necessary to mineralize it artificially. The biological role of most macroelements and trace elements contained in water has been studied rather well [1, 2].

Insufficient intake with water of some minerals could have an adverse effect on both its organoleptic properties and a number of physiological functions of the body [8]. For example, deterioration of organoleptic properties of water related to its demineralization leads to decrease in "drinking requirement" and in some cases there is total abstinence from water [4]. Long-term intake of desalinated water could lead to impairment of fluid-electrolyte metabolism and certain diseases. Thus, considerable biochemical changes in blood composition have been discovered, as well as increased brittleness of bones of polar workers who used glacier melt for drinking for a year [5]. Analogous data are submitted by authors who investigated the effects of water with low mineral content from some therapeutic springs [6]. There is information to the effect that there is greater morbidity referable to digestive organs among individuals who consumed glacier melt for long periods of time [7]. There are data indicative of morphological changes in the gastrointestinal tract under the influence of distilled water, which are related to escape of salts from the mucosa. Long-term intake of desalinated water could also lead to a mineral deficiency and onset of related diseases. It has been established, for example, that water plays the leading role in etiology of diseases related to insufficient intake by man of such trace elements as fluorine and iodine [8, 9].

When man is exposed to particularly extreme conditions (for example, high-altitude mountaineering, at polar stations, in spaceflights) higher physical demands are made of his body. In this case, providing him with a good quality potable water and nutrients consistent with hygienic requirements acquire an important role. For this reason, most hygienists in our country and abroad recognize the fact that water must be enriched with minerals [10, 11]. However, methods of artificial mineralization have not found wide use, with the exception of fluoridation of water.

Investigation of different methods of mineralizing recycled water has shown that the promising ones for spaceflight conditions are those based on use of salts in the solid phase. We can mention, among them, mineral filters in a water "channel" and salt tablets. To improve glacier melt that is to be used as drinking water by mountain climbers, enrichment of water with use of tablets is the most promising method.

Our objective here was to artificially mineralize glacier melt intended for drinking purposes for mountain climbers, in order to improve its organoleptic properties and have it approximate the tap water in Moscow by adding salt tablets.

Methods

On the basis of our studies, we developed a special method of adding salt to water, which included the main macroelements and trace elements inherent in natural potable water, with use of Aquasol type tablets packaged in a special way in foil and polyethylene. One tablet weighing 0.7 g was dissolved in 2 ℓ water, and at room temperature it took an average of 5-10 min for it to dissolve while stirring the water. For enrichment of 2 ℓ water, the tablet contained NaCl (0.3 g), $MgSO_4 \cdot 7H_2O$ (0.392 g), KI (0.00002 g) and NaF (0.004 g). The tablets are prepared from mixtures of the above chemicals using the Engler firm's laboratory tablet press at a pressure of 1200 kg/cm^2. The salt tablets are packaged (10/package) by the Servak packaging machine. The method was evaluated by analyzing the answers of participants to a specially prepared questionnaire.

Results and Discussion

The physicochemical composition of distilled water is close to tap water in Moscow after artificial mineralization, with regard to the basic parameters: hardness 2.0 mg-eq/ℓ; Mg^{2+} 23.6 mg/ℓ; SO_4^{2-} 72.5 mg/ℓ; Cl^- 90.8 mg/ℓ; pH 6.05; alkalinity 0.2 mℓ; I 10 μg/ℓ; F 0.8 mg/ℓ; Na^+ 10 mg/ℓ; K^+ 4 mg/ℓ; transparency 30 cm; taste 0-1 score, odor 0 score.

The final stage of our study was a test of the proposed method of artificial mineralization of glacier melt during a summertime high-altitude expedition on the Pamirs in 1981 and the Everest-82 expedition. Analysis of the answers to the questionnaire charts of 22 participants of the summer expedition enabled us to conclude that, on the whole, all of the participants in the expedition who used salt tablets for addition to glacier melt, tea, coffee and cocoa gave a positive rating. They considered this method to be convenient and recommended it for the Everest expedition. Analysis of questionnaire

answers and medical monitoring of 17 participants in the Everest-82 expedition, who added salt tablets to glacier melt, revealed that virtually all of the sportsmen rated this method of mineralization well. According to the mountain climbers, the flavor of the tablet-enriched water was much better than that of glacier melt. The treated water had no extraneous odor or aftertaste.

The mountain climbers recommended broader use of salt tablets to improve the taste of drinking water during high-altitude mountain climbing expeditions. The set of medical tests revealed that use of Aquasol tablets did not elicit changes in physiological functions of the mountaineers.

All this enables us to recommend the above method of artificial mineralization of glacier melt for use during high-altitude mountain climbing expeditions.

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